FEB 26 1931

VOLUME 11 NUMBER 2

ARCHIVES OF PATHOLOGY

EDITORIAL BOARD

LUDVIG HEKTOEN, Chicago

JAMES EWING, New York
S. B. WOLBACH, Boston
ALFRED STENGEL, Philadelphia
WILLIAM OPHÜLS, San Francisco
W. G. MacCALLUM, Baltimore
OSCAR T. SCHULTZ, Evanston, Ill.

FEBRUARY, 1931

PUBLISHED MONTHLY BY AMERICAN MEDICAL ASSOCIATION, 535 NORTH DEARBORN STREET, CHICAGO, ILLINOIS. ANNUAL SUBSCRIPTION, $8.00

Entered as Second-Class Matter, Jan. 20, 1926, at the Postoffice at Chicago, Illinois, Under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in the Act of Feb. 28, 1925, authorized Jan. 27, 1926.

CONTENTS OF FRE[illegible] MBER

JANUARY, 1931.

ARCHIVES OF PATHOLOGY

VOLUME 11 FEBRUARY, 1931 NUMBER 2

THE ENTEROCHROMO-ARGENTAFFIN CELLS *

S. B. PESSIN, M.D.
WAUWATOSA, WIS.

The rôle of chromo-argentaffin cells in inflammatory processes has not been defined. A histologic investigation was undertaken with this end in view, with especial reference to the part played by the argentaffin cells in acute, subacute and chronic inflammations of the intestinal tract, in particular of the appendix. While it seems conclusive that the argentaffin cells give rise to the carcinoids of the intestinal tract, no definite conclusion has been reached with regard to their significance in inflammatory processes.

LITERATURE

Among the epithelial cells of the gastro-intestinal mucosa, there are a variety of granular epithelial elements of which the morphology, origin, function and pathologic signficance have been of much interest since their first description by Paneth [1] in 1888 and Bizzozero [2] in 1892. Somewhat later, Trautmann [3] and others verified the investigations of Paneth, and spoke of these cells as the "granule cells of Paneth."

Kultschitzky [4] observed other granular cells in the intestinal mucosa, the morphology and staining properties of which were unlike that of the "granule cells of Paneth." With Ehrlich-Biondi stain (acid fuchsin, orange and methyl green), the granules of the cytoplasm were colored red, and therefore he designated them as the "cells with acidophil granules." He noticed that the granules always occupied the basilar portion of the cell.

Schmidt [5] found cells similar to those discovered by Kultschitzky

* Submitted for publication, June 30, 1930.

* From the Department of Pathology, Marquette University, Milwaukee, and Milwaukee County Hospital.

1. Paneth, J.: Ueber die sezernierenden Zellen des Dünndarmepithels, Arch. f. mikr. Anat. **31**:113, 1888.

2. Bizzozero, G.: Ueber die Schlauchformigen Drüsen des Magen-Darmkanals und die Beziehung ihres Epithels zu dem Oberflaschenepithel der Schleimhaut, Arch. f. mikr. Anat. **40**:325, 1892.

3. Trautmann, G.: Zur Kenntnis der Panethschen Kornzellen bei den Säugetieren, Virchows Arch. f. path. Anat. **151**:261, 1897.

4. Kultschitzky, N.: Zur Frage über den Bau des Darmkanals, Arch. f. mikr. Anat. **49**:7, 1897.

5. Schmidt, J. E.: Beiträge zur normalen und pathologischen Histologie Zellarten der Schleimhaut des menschlichen Darmkanals, Arch. f. mikr. Anat. **66**:12, 1905.

in the crypts of Lieberkühn, and was the first to give a complete description of their morphologic characteristics. When the tissues were fixed in Müller's solution plus formaldehyde, the basal portion of the cell stained intensely yellow. He found that the nuclei of argentaffin cells were larger than the nuclei of the adjacent cells of the glands of Lieberkühn. Schmidt named these cells "yellow cells." He also noticed similar cells in the underlying network of nerves and concluded that these periglandular "yellow cells'" migrated from the glands of Lieberkühn.

Ciaccio,[6] studying independently, found such cells in the stomach and the duodenum in the guinea-pig and the dog. He demonstrated vacuoles in the granular portions of the cytoplasm.

For a time the interest aroused by the observations of Kultschitzky and Schmidt subsided, but attention was again awakened when Huebschmann,[7] while studying the carcinoids of the appendix, noticed cells with morphologic and staining characteristics similar to those of the cells of Kultschitzky and Schmidt. Further investigation convinced him that the carcinoids originated from these cells and from the "granule cells of Paneth."

Masson [8] also examined carcinoids; he found that they were composed mainly of cells corresponding to those described by Kultschitzky and Schmidt. He demonstrated the reducing property of the granules to ammoniacal silver, and as a consequence of a predilection for silver, he named the cells "argentaffin cells." Masson was convinced that the argentaffin cells were the same as the cells of Kultschitzky, Schmidt and Ciaccio.

Recent investigators, Cordier,[9] Forbus,[10] Hamperl,[11] Eros,[12] Sprafke [13] and others, verified the morphologic observations of Masson, but they disagreed with him, as well as among themselves, concerning the origin, function and pathologic significance of these cells.

---

6. Ciaccio, C.: Sur une nouvelle espece cellulaire dans les glands Lieberkuhn, Compt. rend. Soc. de biol. **60**:76, 1906.

7. Huebschmann, P.: Sur le carcinome primitive de l'appendice vermiculaire, Rev. méd. de la Suisse Rom. **30**:317, 1910.

8. Masson, P.: Tumeurs endocrinis de l'appendice, Presse méd. **22**:25, 1914.

9. Cordier, R.: Contribution a l'étude de Ciaccio-Masson et la cellude de Paneth, Compt. rend. Soc. de biol. **88**:1227, 1923.

10. Forbus, W. D.: Argentaffin Tumors of the Appendix and Small Intestine, Bull. Johns Hopkins Hosp. **37**:130, 1925.

11. Hamperl, H.: Ueber die gelben (chromaffinen) Zellen in gesunden und kranken Magendarmschlauch, Virchows Arch. f. path. Anat. **266**:509, 1927.

12. Eros, G.: Ueber die argentaffinen Zellen der Schleimhaut des Magen und Darmtraktes, Frankfurt. Ztschr. f. Path. **36**:402, 1928.

13. Sprafke, H.: Untersuchungen über die argentaffinen Zellen in der Schleimhaut des Wurmfortsatzes und ihre Beziehungen zur Entstehung der sogenannten Karzinoide, Frankfurt. Ztschr. f. Path. **35**: 302, 1927.

Many hypotheses have been formulated to account for the origin of the enterochromo-argentaffin cells, yet the genesis of these cells still remains obscure.

The early investigators made only feeble attempts toward investigative proof, but later researches have thrown some light on the histogenesis of these granule cells. Masson's [14] embryologic studies led him to believe that the chromo-argentaffin cells are of entodermic origin. He demonstrated their appearance in the intestinal mucosa of man about the fourth month of fetal life. Parat confirmed Masson's observations, but Kull,[15] who studied the cells in the chick embryo by the mitochondrial method (he did not use ammoniacal silver), reported that the chromaffin cells originated from mesenchyme cells that had invaded the epithelium. Masson refuted Kull's report by contending that the mitochondria of the connective tissue and the chromaffin granules of the chromo-argentaffin cells differ widely in both size and staining reactions.

Danisch [16] showed that the chromo-argentaffin cells arise from the celiac ganglion and migrate into the gastro-intestinal mucosa about the fourth month of fetal life. He found these cells in the submucosa in the tenth week of embryonal life, but he was unable to demonstrate argentaffin cells in embryos of six weeks. Masson [8] urged the rejection of Danisch's observations because the latter had used macerated material and had stained his sections by Agdhur's silver technic. Agdhur's silver technic colors certain chromaffin cells of the sympathetic paraganglions, but does not color the argentaffin cells specifically.

As a result of two pathologic observations, Masson stressed the entodermic origin. He found many argentaffin cells in regenerating epithelium of chronic gastritis, and argentaffin cells are always mixed with cylindric cells in the carcinoids of the intestinal tract.

Hamperl [11] did not think that the argentaffin cells belong to the chromaffin system; he attributed their origin to a faulty differentiation during the regeneration of the epithelium after inflammation.

Many workers who found similar cells in the pancreatic islands, suprarenal glands and hypophysis concluded that these cells belong to the chromaffin system. Tang [17] expressed the belief that the cells might be a type belonging to the "granule cells of Paneth."

14. Masson and Berger: Sur un nouveau mode de secretion interne la neurocrinie, Compt. rend. Acad. de sc. **176**:1748, 1923.

15. Kull, H.: Die chromaffinen Zellen des Verdauungstraktes, Ztschr. f. mikr. anat. Forschung. **2**:163, 1925.

16. Danisch, F.: Zur Histogenese der sogenannten Appendixkarzinoide, Beitr. z. path. anat. u. z. allg. Path. **72**:687, 1923-1924.

17. Tang, E. H.: Ueber die Panethschen Zellen sowie die gelben Zellen des Duodenums bein Schwein und den anderen Wierbeltieren, Arch. f. mikr. Anat. **96**:182, 1922.

Block claimed that the "granule cells of Paneth" aided the digestion of milk. Klein [18] suspected that the granules of Paneth's cells were zymogen granules. Zimmerman [19] maintained that they were serous cells. Bensely considered them as serous zymogen cells, and Macallum as prozymogen cells. Bizzozero [2] contended that they were young mucin cells.

Kultschitzky [4] was certain that the cells possessed some functional attributes in the process of digestion. He noticed a certain number of these cells in his normal dogs. When a dog was subjected to a diet wholly of meat, Kultschitzky found that the number of argentaffin cells increased; however, when he starved the dogs and cleared the gastro-intestinal tract with magnesium sulphate, he was unable to demonstrate a single argentaffin cell throughout the entire gastro-intestinal tract.

Schmidt [5] maintained that the argentaffin cells possess some nervous functional element. Ciaccio,[6] because of their chromaffinity, hypothecates that these cells might produce epinephrine which is poured into the gastro-intestinal tract. However, the marked and almost specific reaction of these cells to ammoniacal silver suggests that the substance secreted and true epinephrine are not similar.

Masson,[8] in his early papers, contended that the argentaffin cells possess an endocrine function. In his later works, while studying obliterated appendixes, Masson observed certain minute tumors known as neurinomas or neuromas. In the center of these neuromas, he always demonstrated argentaffin cells. It is certain that neuromas originate from the periglandular plexus. In normal and inflamed appendixes, he noticed a budding of the glands of Lieberkühn and the pushing out of argentaffin cells from a ruptured basement membrane. Masson was able to find more periglandular argentaffin cells in appendixes with pathologic histories. He also found that wherever the periglandular argentaffin cells were abundant, the periglandular nerves were hypertrophied and had even undergone hyperplasia. Thus, by correlating the glandular and periglandular argentaffin cells with the nervous hypertrophy and hyperplasia, Masson concluded that the neuromatosis of certain appendixes was influenced by the extraglandular argentaffin cells.

In short, Masson's explanation is that the periglandular argentaffin cells are the glandular argentaffin cells that have migrated from the crypts. Whether the periglandular cells possess some nutritive or irritative influence on the periglandular plexus to cause them to grow is not definitely known. However, Masson's work proved that the existence of these neuromas depends on the presence of the argentaffin

18. Klein, S.: On the Nature of the Granule Cells of Paneth in the Intestinal Glands of Mammals, Am. J. Anat. **5**:315, 1906.

19. Zimmerman, K. W.: Beiträge zur Kenntnis einiger Drüsen und Epithelien, Arch. f. mikr. Anat. **52**:552, 1898.

cells. When the argentaffin cells degenerate, the neuromas also degenerate. Masson [20] thought it fitting to designate the activity of the periglandular argentaffin cells as "a neurocrine function," because these cells are able to promote and maintain a well nourished and growing periglandular plexus.

According to Kull,[15] the argentaffin cells possess two Golgi processes, one apical and the other basal; but Cowdry [21] stated that the Golgi apparatus is connected with the pole of discharge. Furthermore, in certain carcinoids there are cavities filled with a homogeneous colloid liquid and bordered by argentaffin cells. This might indicate that the argentaffin cell secretes something from its apical pole. From the preceding observations one may conclude that these cells have an exocrine function. However, Masson said, "This does not exclude a concomitant endocrine function. The liver cells normally exhibit polarities external and internal; the pancreatic cell exhibits them successively."

Cordier [9] waived the belief that the argentaffin cells have an endocrine function, but he was certain that they have an exocrine function, for after an injection of pilocarpine the granularity of the cells lessened or disappeared altogether. Masson did not deny the granular diminution after the injection of pilocarpine, but he maintained that Cordier had been unable to demonstrate in which direction the product that results from the destruction of the argentaffin granules is excreted.

Embryologic investigations convinced Danisch [16] that since the argentaffin cells originate from the solar plexus they must possess some paraganglionic function.

I have observed that as long as the chromo-argentaffin cells are in contact with the basement membrane of Lieberkühn's glands, the granules are always aggregated at the base. Such basal massing indicates, as Masson said, an "endotropic polarization," and thus supports the logical conclusion that these cells possess an endocrine function. Entz long ago proclaimed the hypothesis that in every organ, as well as in the gastro-intestinal tract, endocrine cells must exist. Perhaps the chromo-argentaffin cells are the cells of Entz's hypothesis.

MATERIAL USED FOR STUDY

At the Milwaukee County Hospital, tissues from forty-five necropsies and sixty-six appendixes removed at operation were studied. The necropsy material consisted of all portions of the gastro-intestinal tract, including the appendix, pancreas, suprarenal glands, paraganglionic tissue and the hypophysis. The duodenum of the rabbit and that of the guinea-pig were also studied.

---

20. Masson, P.: Carcinoids (Argentaffine-Cell Tumors) and Nerve Hyperplasia of the Appendicular Mucosa, Am. J. Path. **4**:181, 1928.

21. Cowdry, R.: The Reticular Material as an Indicator of the Physiologic Reversal in Secretory Polarity in Thyroid Cells of Guinea-Pig, Am. J. Anat. **30**:25, 1922.

Five hundred and forty serial slides were prepared. Each slide contained from ten to forty sections, and the following were considered: the normality, the pathologic appearances and the postmortem changes of the tissues, the proportional nervous, lymphoid and glandular character of the appendixes, and the morphology, staining, situation and distribution of the argentaffin cells.

THE SILVER STAINING METHOD

With the Ehrlich-Biondi-Heidenhain method, the granules stained red; with Müller's solution plus formaldehyde, yellow; with Masson's method, black, and with basic blues, greenish-blue. The chromo-argentaffin cells were demonstrated best by Masson's method, which is as follows:

1. Fix tissue (fresh tissue, if possible) in Bouin's solution three days. (Bouin's solution: formaldehyde solution, 10; trinitrophenol, 30; acetic acid, 2.)
2. Transfer to neutral solution of formaldehyde for from one to two months.
3. Cut section from 1 to 2 mm. thick.
4. Wash in distilled water from twelve to twenty-four hours.
5. Transfer to ammonia water for from twelve to twenty-four hours (500 cc. of distilled water with 2 drops of ammonia).
6. Place in Fontana solution half diluted for six days, excluding all light.
7. Place in reduction fluid for from six to eight hours (formaldehyde solution, 5; water, 50; pyrogallic acid, 5).
8. Embed in paraffin.

Most of the sections were stained by this method. The surgical department was supplied with small bottles containing Bouin's solution which were labeled "for appendixes and other gastro-intestinal tissues." Thus it was assured that fresh tissue was placed in a very efficient fixing solution. About thirty of the appendixes removed at operation were fixed by this method; the remaining thirty-six were sent to the laboratory in 10 per cent formaldehyde and then transferred into Bouin's solution. About 75 per cent of the necropsy material was placed directly in Bouin's solution; the remaining 25 per cent was first placed in 10 per cent formaldehyde and then transferred to Bouin's solution.

Silver is the most capricious stain for microscopic study. One is often at a loss to explain adequately the variability and the fluctuation of the same type of cells toward impregnation with silver. Unless one enforces a careful technic, the impregnation with silver yields many artefacts. Great care was taken in preparing the solutions, and strict attention was given to the reduction time. Sections that showed too much precipitation and thus manifested artefacts were discarded, even though they contained extraglandular argentaffin cells.

DISTRIBUTION OF THE ARGENTAFFIN CELLS

The enterochromo-argentaffin cells are distributed inconstantly throughout the entire gastro-intestinal tract. They are found singly or in pairs among the columnar cells of the stomach, duodenum and appendix. Occasionally, they may be demonstrated in the cardiac portion of the stomach and the large intestine. They are also found singly or in groups of from three to twenty-five cells (fig. 1) in the periglandular plexus of nerves, but cannot be demonstrated in the lymphoid tissue or in the external nerve plexus. Thus, two distinct classes should be considered: (1) glandular enterochromo-argentaffin

cells and (2) periglandular enterochromo-argentaffin cells. Silver-reducing cells that simulate the enterochromo-argentaffin cells were demonstrated in the islands of Langerhans of the pancreas, and in the suprarenal cortex, hypophysis and paraganglionic tissue, but it was found that their staining and morphologic characteristics differ from the enterochromo-argentaffin cells. The argentaffin cells of the islands of

Fig. 1.—A group of eight periglandular argentaffin cells of the epithelial type observed in a section of the appendix. The light-staining nuclei are almost centrally located.

Langerhans are smaller, and their nuclei are round, distinct and centrally located; they reduce silver very mildly. The argentaffin cells of the suprarenal glands contain fine granules distributed throughout the cytoplasm; the granules stain dark brown, and the nuclei are not as definite as those of the cells found in the islands of Langerhans. Nevertheless, the argentaffin cells of the pancreatic islands and those

of the suprarenal gland are somewhat similar. The argentaffin cells of the two hypophyseal glands reduce silver to a greater degree than the cells of the suprarenal glands and the islands of Langerhans. The paraganglionic argentaffin cells reduce silver with almost as great intensity as do the argentaffin cells of the intestinal tract; however, they can be easily recognized by their processes.

Fig. 2.—Three argentaffin cells in a transverse section of a gland of Lieberkühn. The appendix was obtained at operation from a patient 7 years of age and showed subacute appendicitis.

GLANDULAR ENTEROCHROMO-ARGENTAFFIN CELLS

The glandular argentaffin cells are scattered among the cylindric cells that line the gastro-intestinal tract. They are more abundant in the crypts of Lieberkühn, where from one to twenty-eight argentaffin cells may be counted in 100 microns of tissue. From about 70 per cent to 90 per cent of these cells are found at the bottom of the crypts.

Masson gave the average as between five and ten cells per crypt. From one to three (fig. 2), rarely four, argentaffin cells can be seen in the transverse sections of the glands of Lieberkühn, the average being one or two cells. They are less frequent in the upper portions, but may be found as high as the tip of the villus.

The form of the glandular enterochromo-argentaffin cell is fairly constant. The cell may be conical (fig. 3), pyramidal (fig. 4) or flask-

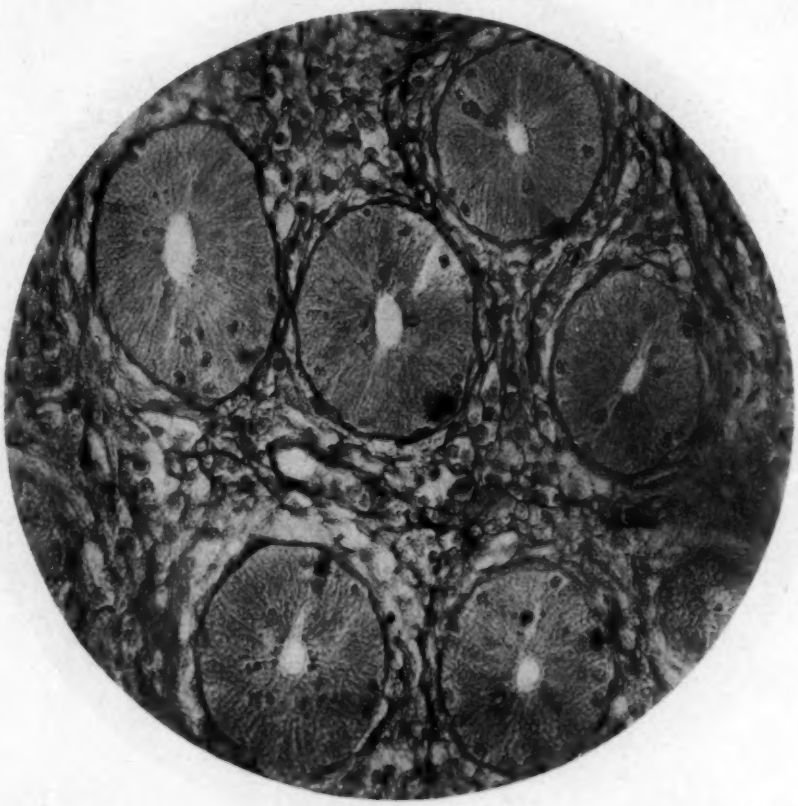


Fig. 3.—Five slender, conical glandular argentaffin cells. The nuclei contain very little chromatin granules. Many sections were prepared from this appendix, and no supranuclear granulations were found. The appendix was obtained at necropsy from a man 71 years of age.

shaped (fig. 5). However, the size of the cell frequently varies. Much depends on the species and the region in which it is found. I have seen various sizes in the same section and even in the same gland. In comparison with the contiguous cylindric epithelial cells that line the glands of Lieberkühn, it is usually shorter and wider (fig. 4), but it may

be as tall and as narrow as the cylindric cells. Usually the apical portion is not seen to reach the lumen of the gland, and is lost among the cylindric cells, but occasionally the apex may be seen reaching the lumen (fig. 5). The average size of the argentaffin cell is 16 microns in height and 9 microns in width; the cylindric cell is 20 microns high and 4 microns wide.

Fig. 4.—Seven pyramidal glandular enterochromo-argentaffin cells in an appendix obtained at autopsy from a 21 year old patient who died of lobar pneumonia.

Cytoplasm.—The cytoplasm is clear and homogeneous and does not stain as well as the cytoplasm of the cylindric cells. The cytoplasm below the nucleus contains many granules. The presence of granules in the basal portion of the cytoplasm is constant, but their presence in the supranuclear region is very inconstant. Above the nucleus, they may be absent entirely, but frequently one finds a few fine granules scattered

in the vicinity of the upper pole of the nucleus (figs. 4 and 5). More often they are found at the sides and the adjacent portions above the nucleus (fig. 6); here the granules may be as numerous as in the basal pole of the cell. Occasionally, the entire cytoplasm is filled with argentaffin granules. When such a cell is found, it appears as a black pyramid-shaped object with a central light area, the nucleus (Masson's method).

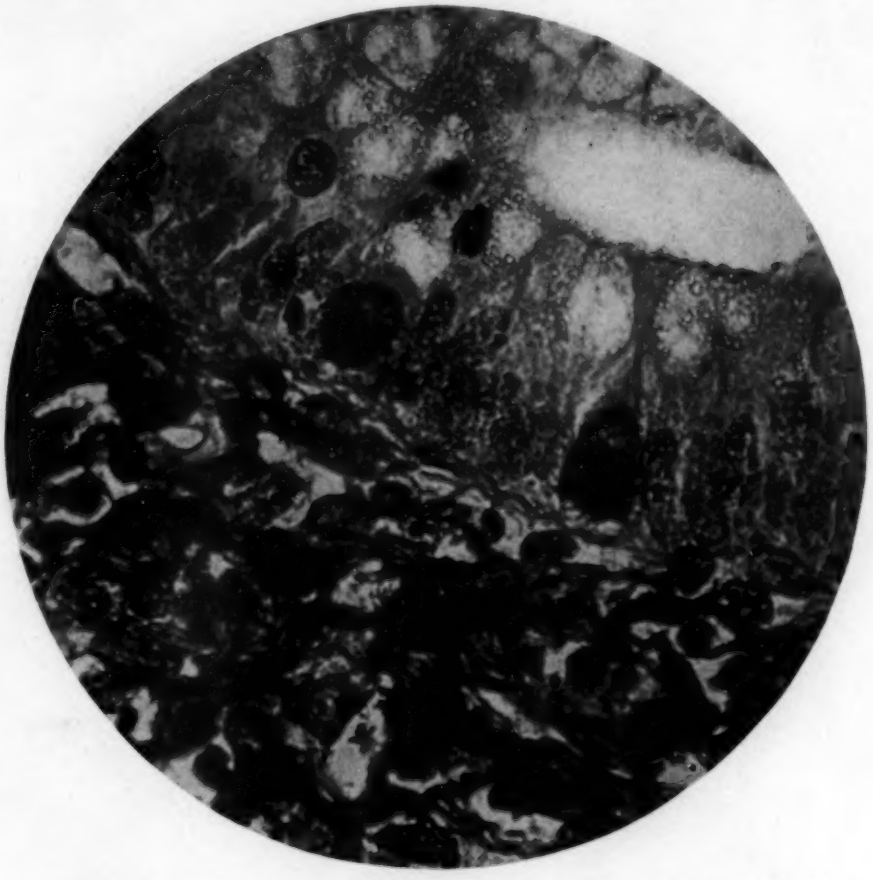


Fig. 5.—Two glandular argentaffin cells of the appendix. The one located in the right hand portion of the field is a flask-shaped cell the entire outline of which is plainly visible and the apical portion of which is seen to reach the lumen.

As the granules vary in quantity, so they also vary in size and staining characteristics. Much depends on the technic employed. Some granules do not reduce silver or rather reduce it sluggishly, but stain well with acid dyes; however, the great majority of the cells contain granules that reduce ammoniacal silver with marked intensity. This

inconstant reduction may be seen in the same section or even in the same crypt. Masson thought that the different sizes and the variable staining characteristics are due to the different evolutionary stages of the granules. The cytoplasm also contains a few vacuoles, which are usually located in the basal pole of the cell. These vacuoles are sometimes filled with doubly refractory lipoids and they stain with sudan III

Fig. 6.—A high power view of an argentaffin cell the nucleus of which is surrounded by argentaffin granules.

and osmic acid. There are other vacuoles that are stainless, which perhaps is due to the degeneration of the granules; there may also be empty spaces as a result of the extrusion of the granules.

Nucleus.—The nucleus is round or oval and appears swollen. It is situated on a higher plane than the nucleus of the cylindric cell of the glands of Lieberkühn. It is never in contact with the basement

membrane, but is located almost in the center of the cell. It may be smaller or larger than the nucleus of the cylindric cell; usually they are about equal in size, but the nucleus of the argentaffin cell is somewhat broader. The nucleoplasm is clear and vesicular, and contains a fine sprinkling of chromatin substance that possesses an affinity for silver. In an argentaffin cell that is loaded with granules, the nucleus seems to bubble out from the black granular mass. The nucleus contains a nucleolus and sometimes one or two karyosomes.

PERIGLANDULAR ENTEROCHROMO-ARGENTAFFIN CELLS

Sprafke [13] stated that the periglandular type of argentaffin cells is found less frequently than the glandular type; however, I have observed that the frequency of both types is about equal. In an examination of 107 appendixes (excluding 4 obliterated appendixes) I found that 43 showed glandular argentaffin cells; 37 periglandular argentaffin cells; 21 both glandular and periglandular cells; 22 the glandular type only, and 16 the periglandular type only.

The periglandular argentaffin cells are usually located near the crypts or embedded in a hypertrophied and hyperplastic periglandular nerve plexus. Very rarely are they seen in contact with the basement layer of the epithelial lining. They are not found in the lymphoid interstices nor beyond Meissner's plexus, but in obliterated appendixes they are seen near the inner muscular coat, singly, in pairs or in groups of from three to twenty-five cells (fig. 1).

Morphologically, the periglandular chromo-argentaffin cells vary considerably. They possess no constant form nor almost constant size, as do the glandular argentaffin cells. The periglandular cells may be pyramidal, spheroidal or polyhedral; they may be smaller or three times larger than the largest glandular argentaffin cells. Usually the periglandular cells are about one and one-half times larger than the glandular type.

Masson classified the periglandular argentaffin cells into four types:

1. Neurocrine: This type is made up of polygonal or rounded cells, the cytoplasm of which is very granular and hollowed out by vacuoles containing lipoids.
2. Schwannian: The nucleus of the Schwannian cell is enclosed in neuroglial syncytium; the cytoplasm contains few granules.
3. Ganglion: The ganglion argentaffin cell has the contour of a ganglion cell; the nucleus is vesicular and contains a nucleolus.
4. Intestinal: The cells of this type are arranged in rosets; only the basal portion of the cytoplasm contains granules.

The fourth type could not be demonstrated in the periglandular or subglandular tissues. All of the periglandular argentaffin cells that were observed contained granules, in greater or lesser degrees, throughout the cytoplasm; polar collections of granules in these cells were not seen.

In this paper, it is not urged or even suggested that Masson's classification be modified or revised. Masson's investigations of the argentaffin bodies have been extensive, and his publications regarding them have not yet been equaled. However, as an expression of diligent observation, I must classify the periglandular argentaffin cells as I saw

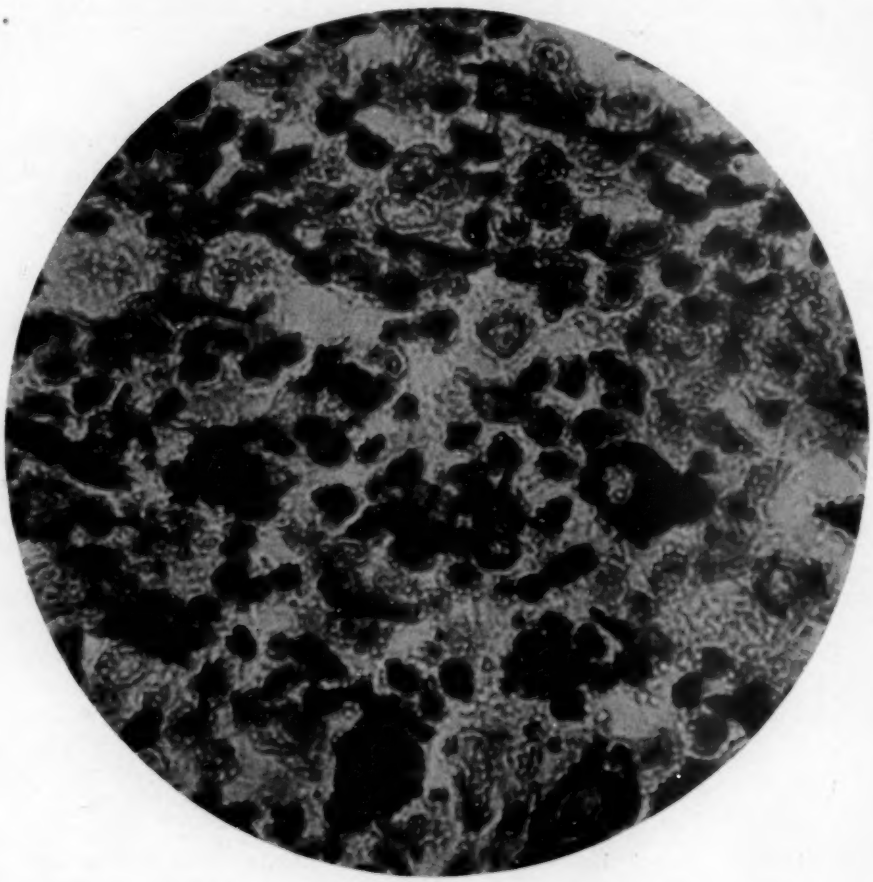


Fig. 7.—High power of the epithelial type of the periglandular argentaffin cells.

them under the microscope. They may be considered as of the following types: (1) epithelial, (2) syncytial and (3) ganglionic.

Epithelial Type (fig. 1).—The epithelial type of the periglandular argentaffin cells is always in close proximity to but not contiguous with the basement membrane of the cylindric cells that line the gastro-intestinal tract. It is large, spheroidal and sometimes pyramidal. The outline is smooth, with no processes or pseudopods. The cytoplasm contains a

more or less uniform and abundant distribution of various-sized argentaffin granules, but occasionally may show a slight concentration in one or two places of the cytoplasm. The entire outline of the nucleus is seldom seen; this is due to the abundance of granules in the cytoplasm. Frequently the nucleus is entirely concealed. Whenever the nucleus is seen, it is found almost centrally located and appears as a lightly stained round or oval body, sprinkled with a fine chromatin substance.

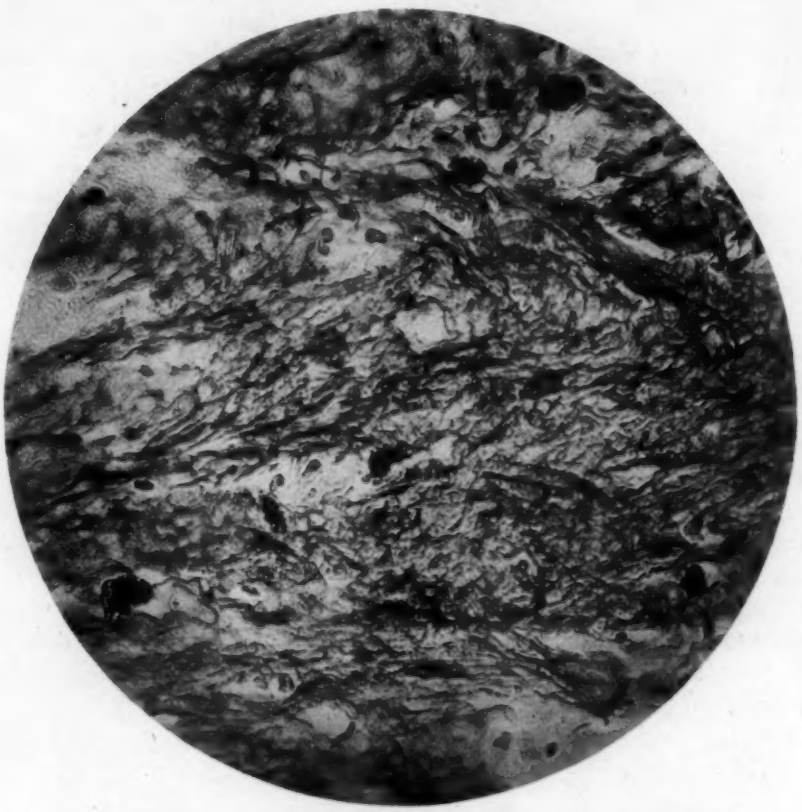


Fig. 8.—Obliterated appendix showing eleven periglandular argentaffin cells of the syncytial and ganglionic types.

Syncytial Type.—This cell possesses no distinct cytoplasmic covering, and can only be recognized as a defined granular area with an almost centrally located, lightly staining nucleus. The granules are variable in size and amount. Sometimes the cell contains only about a dozen granules around the nucleus, but usually the entire cell is densely filled with granules. Frequently the nucleus is seen within a group of neuroglial fibers, and appears to be in close relation with these fibers.

According to Masson, "These argentaffin cells are no longer individualized, they form an integral part of the Schwannian syncytium."

Ganglionic Type (fig. 8).—The ganglionic type is moderately granular. The outline of the cell is well evident and shows one or two processes. The nucleus is vesicular, stains lightly and may contain one or two nucleoli.

The last two types are usually seen farther from the crypts and more into the depths of the periglandular plexus. Their most frequent habitat is the axial connective and neuroglial tissues of the obliterated appendixes. Three of the four obliterated appendixes that were examined contained both the syncytial and the ganglionic type.

MIGRATION

Masson efficiently demonstrated and described the migratory tendencies of the argentaffin cells. Migration, according to Masson, is possible by the budding of the tip of the gland of Lieberkühn. Budding begins with an increase of nuclei at or near the tip of the crypt, and the resulting pseudopod enlarges and appears to contain a multinucleated syncytial mass. As soon as the bud begins to separate from the crypt, the cytoplasm becomes more and more granular. When the bud has broken, the syncytial mass of cytoplasm, nuclei and granules differentiates into the various types of periglandular argentaffin cells.

Sprafke,[13] Hamperl,[11] and Eros [12] and others have not demonstrated such an interesting phenomenon. I was unable to see the least possible suggestion of budding. However, I am inclined to surmise that the epithelial periglandular argentaffin cells originate from the glandular argentaffin cells, but thus far the work done has been insufficient to warrant a substantial account of their presence in the periglandular plexus.

CLINICAL SIGNIFICANCE

Clinically, the significance of the argentaffin cells is perhaps of small importance. The condition known as pseudo-appendicitis may be explained by the "phenomenon of Masson," e. g., the migration of the glandular argentaffin cells into the nerve plexus, causing it to hypertrophy. These hypertrophied and hyperplastic nerve elements, known as neuromas, may produce pain and cause one to suffer from an apparently normal, noninflamed appendix.

Another interesting fact that is worth mentioning is that the enterochromo-argentaffin cells are the genetic cells of the carcinoids of the gastro-intestinal tract. Masson, Forbus, Sprafke and others have already ascertained the argentaffin origin of the carcinoids. The following is a description of a carcinoid that was recently studied.

The tumor was located 1 cm. from the distal end of the appendix. It was 6 mm. in diameter, yellowish and firm. The lumen of the appendix in this region was almost entirely obliterated. Microscopically, the carcinoid was seen to occupy the mucosal and submucosal regions. The cells were arranged in nests and strands separated by fibrous septums. Now and then one could see solid masses of cells surrounded by a fibronervous capsule (fig. 9). There were occasional areas of homogeneous substance enclosed by epithelial cells. The cells were round or oval and slightly variable in size; those that were located in the center of the nests were round and somewhat smaller than the cells in the periphery. The

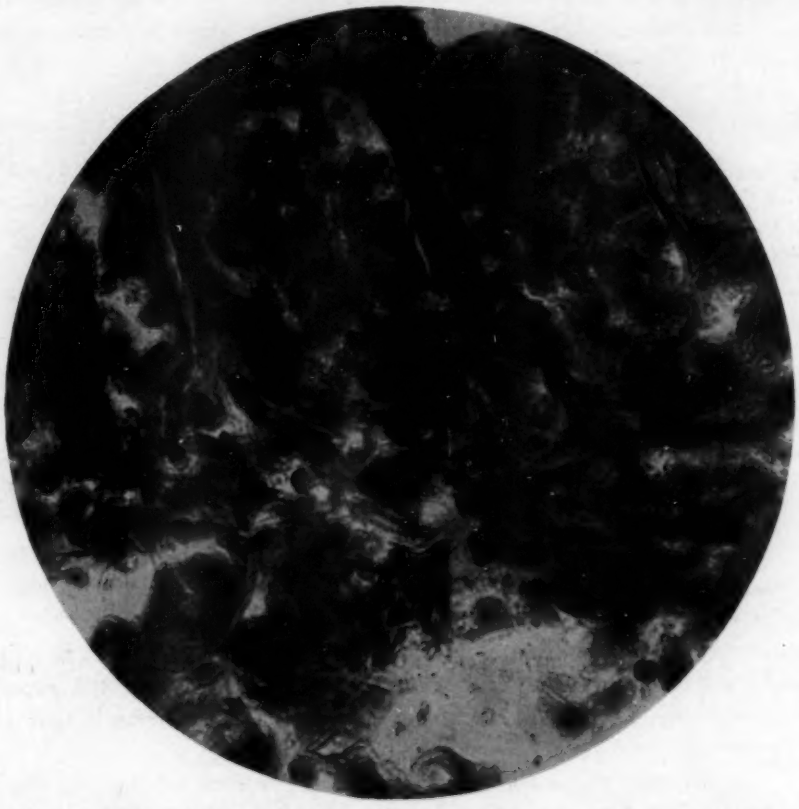


Fig. 9.—Carcinoid of an appendix showing a solid adenomatous growth. There are light spaces bordered by argentaffin cells. The cells reduced silver sluggishly They stained dark brown with Masson's method.

nuclei were round or oval and vesicular, and contained a moderate amount of chromatin; sometimes nucleoli were seen. The cytoplasm was rather evenly distributed with fine and coarse granules and few vacuoles. The granules reduced silver rather sluggishly and therefore were colored dark brown.

Histologically, there are a few interesting factors that may be mentioned concerning the variability of the argentaffin cells in certain pathologic changes of the appendix.

Sprafke [13] found that in normal appendixes and in those with mild inflammatory changes, the ratio of negative to positive results in examination for argentaffin cells was 3:1, whereas in marked inflammatory appendixes, the ratio was 1:3.

Eros,[12] in almost every instance, was able to demonstrate chromo-argentaffin cells in appendixes the mucosa of which had not undergone severe inflammatory changes. He examined twenty-eight appendixes removed at operation and demonstrated argentaffin cells in all but four. In these, the mucosa was denuded and the submucosa edematous.

The investigations that prompted this paper yielded results as set forth in the accompanying table.

Results of Examination of Appendixes for Enterochromo-Argentaffin Cells, with Relation to Clinical Conditions

	Total	Positive	Negative
Appendixes examined	111	59	52
Appendixes obtained at necropsy	45		
Apparently normal	37	19	18
Obliterated	2	1	1
Chronic fibrous	2	1	1
Atrophic	1		1
Showing acute appendicitis	1	1	
Showing hyperplasia of the lymph follicles	1		1
Showing gross evidence of postmortem changes	1		1
Appendixes obtained at operation	66		
Showing chronic appendicitis	32	21	11
Showing acute appendicitis	20	9	11
Showing subacute appendicitis	8	5	3
Showing gangrenous appendicitis	2		2
Obliterated	2	2	
Normal	2		2

From the results one cannot form definite conclusions. The chronically inflamed appendix demonstrates a predilection of the argentaffin cells for this tissue; the gangrenous and severely inflammatory appendixes are always negative for these cells; the appendixes showing mild and moderately acute inflammatory conditions presented argentaffin cells in 50 per cent of the cases. However, the same is true for the normal appendix.

An attempt was made to associate the presence of the argentaffin cells with the lymphoid character, the glandularity and the nerve distribution, respectively; but since the results were of so fluctuating a nature, a precise statement concerning their relationship cannot be made. It suffices to say that usually when the appendix possessed a scanty periglandular nerve plexus, the argentaffin cells were absent; but when the periglandular argentaffin cells were present, the nerve plexus appeared to be well developed.

Age is a minor factor in the distribution of the chromo-argentaffin cells of the intestinal tract. Masson claimed that the argentaffin character of the appendix lessens with age; the optimum, according to

his investigation, is from fifteen to twenty years. Others contend that the age factor plays a minor rôle in the argentaffin cellularity of the appendix. I found an abundant distribution of argentaffin cells in the appendix of a man 71 years of age, whereas on several occasions I was unable to demonstrate them in the appendixes of youths.

The number of positive results in the examination of apparently normal appendixes obtained at necropsy was, in comparison with the numbers reported by other investigators, rather low. Slightly over 50 per cent presented argentaffin cells in the mucosa or submucosa. Perhaps the slight postmortem change destroys the argentaffin granules.

SUMMARY

The literature tracing the development of the chromo-argentaffin cells has been reviewed in chronologic order.

Attention is called to the fact that the Kultschitzky-Schmidt-Ciaccio cells are the same as the chromo-argentaffin cells of Masson.

The glandular argentaffin cells specifically belong to the intestinal tract and may be termed enterochromo-argentaffin cells.

The periglandular argentaffin cells are morphologically so variable and their origin is so uncertain that no definite classification is possible at present.

From the results of this investigation no definite conclusions can be formed concerning the pathologic significance of the argentaffin cells.

EXPERIMENTAL RHEUMATIC LESIONS IN DOGS AND IN RABBITS *

V. H. MOON, M.D.
AND
H. L. STEWART, M.D.
PHILADELPHIA

It is not the purpose in this paper to review the subject of rheumatism. Comprehensive discussions of its various phases have recently appeared.[1] The infectious character of rheumatism is generally accepted, as is also the frequent, if not constant, association of streptococci with rheumatic disease. Opinion is divided as to the exact nature of this association. One interpretation is that streptococci are the etiologic agents, of which the lesions of rheumatism are the pathologic effects. Another interpretation is that the primary etiologic agent has not yet been demonstrated, and that the streptococci are merely secondary invaders, the effects of which may be superimposed on or combined with those of the unknown organism. This interpretation is supported by the belief that the lesions of rheumatism are specific and represent the effects of the infectious agent somewhat as the tubercle does in tuberculosis. The difficulty of reproducing rheumatic lesions in characteristic form experimentally has contributed to the uncertainty regarding the etiology of the condition. Such experimental lesions have been reported by many workers.[2] The evidence presented, however, has not been sufficient to convince every one that the experimental lesions presented the specific features of rheumatism. While conducting experiments on chronic focal infections with streptococci, we obtained results that are of interest because of their bearing on the pathogenesis of rheumatic lesions.

---

* Submitted for publication, July 11, 1930.

* From the Department of Pathology, Jefferson Medical College.

* This work was made possible by funds from the Martin Research Foundation.

1. Cecil; Nichols, and Stainsby: J. Exper. Med. **50**:617, 1929. Clawson, B. J.: Aschoff Nodule, Arch. Path. **8**:664, 1929.

2. Wächter: München. med. Wchnschr. **55**:1101, 1908; Deutsches Arch. f. klin. Med. **96**:493, 1909. Jackson, Leila: J. Infect. Dis. **11**:243, 1912. Coombs; Miller and Kettle: Lancet **2**:1209, 1912. Rosenow and Coombs: Lancet **2**:1692, 1913. Rosenow, E. C.: J. Infect. Dis. **14**:61, 1914. Clawson, B. J.: Etiology of Acute Rheumatic Fever, ibid. **36**:444, 1925. Birkhaug, K. E.: Rheumatic Fever; Bacteriologic Studies of Non-Methemoglobin-Forming Streptococcus, with Special Reference to Its Soluble Toxin Production, ibid. **40**:549, 1927. Small, J. C.: Am. J. M. Sc. **173**:101, 1927. Gross; Loewe, and Eliasoph: J. Exper. Med. **50**:41, 1929.

SOURCE OF MATERIAL

In a case of subacute bacterial endocarditis, a pure culture of a streptococcus of the *viridans* group was obtained from the blood stream during life and from the mitral vegetations at postmortem examination.

The patient, a white mechanic, aged 25, had repeated attacks of rheumatism, which began when he was 15 years of age. The first attack lasted four months; the second, two months; the third attack, five years ago, lasted several weeks. He was subject to frequent attacks of sore throat and tonsillitis. The present illness dated from a severe "cold" contracted five months before. Small, red, painful spots appeared in the skin of the fingers and toes. Increasing dyspnea developed on exertion; there were nausea and vomiting, weakness and decreased appetite and a loss of about 28 pounds (12.7 Kg.) in weight. The maximum cardiac impulse was in the fourth and fifth interspaces 15 cm. to the left of the midsternal line. The heart sounds were loud, with a booming first sound, a soft diastolic murmur and a rough systolic murmur transmitted to the axilla. The pulmonic second sound was increased. The liver extended about 4 cm. below the costal margin. The spleen was palpable. The temperature curve was irregular, with elevations of from 1 to 4 degrees above normal. Moderate anemia developed, with red cell counts ranging from 3,000,000 to 2,400,000. The leukocyte count ranged from 6,000 to 16,800 per cubic millimeter of blood. There were repeated showers of petechiae. The urine contained a small amount of albumin; in some specimens there were coarsely and finely granular casts. Painful swelling developed in the left hand and wrist. This subsided in a few days. A partial unilateral hemiplegia occurred, from which recovery was gradual. The evidences of illness gradually became more marked. Nine weeks after admission death occurred from cardiac failure. Postmortem examination (Dr. B. L. Crawford) showed: vegetative mitral endocarditis, vegetative auricular endocarditis, moderate mitral sclerosis, disseminated perivascular fibrosis of the myocardium, serous pericardial effusion, bilateral bronchopneumonia with edema, multiple infarctions of the spleen, kidneys and myocardium and chronic glomerulonephritis.

A fragment of thrombus from a vegetation on the mitral valve was crushed and suspended in salt solution. This suspension was streaked on blood agar plates. After twenty-four hours these plates contained hundreds of minute, firm, dry, discrete colonies, which did not spread readily when rubbed with a wire loop. The colonies were surrounded by a narrow zone of partial hemolysis, and had a distinct greenish color by transmitted light. An isolated single colony was planted into a flask of ascitic broth, which, on the following day, was used for inoculation of the animals. In broth the organisms tended to adhere in small spherical masses. There was no diffuse turbidity of the broth. Only a few chains and pairs of organisms, isolated from the globular masses, were seen in spreads made from the broth culture. This streptococcus grew readily in dextrose hormone broth and in plain broth to which serum, blood or ascitic fluid had been added. It did not liquefy gelatin. When grown in sugar-free broth to which pure sugars were added, it produced acid on dextrose, lactose, saccharose, maltose, levulose, galactose and inulin. Since streptococci of this group rarely ferment inulin, this reaction was questioned and was verified repeatedly. Litmus milk was acidified and coagulated. Mannite was unchanged.

LESIONS IN INOCULATED ANIMALS

Four healthy, vigorous pups about 10 weeks old were each given the sediment from 2 cc. of a twenty-four hour ascitic broth culture

intravenously. At the same time a focus of infection was made in each by implanting the organism in the peritoneal cavity on a cotton plug by means of a trocar and cannula. These animals will be referred to as D 38, D 39, D 40 and D 41. Four young rabbits, weighing from 875 to 1,000 Gm. each, were inoculated similarly. They will be referred to as R 96, R 97, R 98 and R 99.

Within forty-eight hours each of the pups presented swollen, tender joints. The joint capsules were distended with serous effusion. The arthritis had a definite migratory character. In the joints first involved the swelling and tenderness subsided, and a similar condition developed in other joints. This arthritis tended to subside in about ten days. No purulent arthritis developed. In a few joints there was slight residual stiffness. The temperature of these animals ranged from 101 to 103.4 F. The leukocytic count ranged from 10,000 to 24,000. The hemoglobin and red cell count declined 30 per cent to 40 per cent from normal. The pups lost flesh, ate little and grew more slowly than untreated pups of the same litter.

Two of them manifested peculiar muscular movements. These consisted of frequent spasmodic, jerky, uncoordinated, purposeless movements of the legs and, less noticeably, of the trunk and neck. Having never seen chorea in dogs, we have no basis for comparison, but this was suggestive of the choreiform movements seen in rheumatic children. This manifestation persisted for about a week and subsided gradually.

D 41 was killed and examined fourteen days following inoculation. The right elbow and left shoulder joints were distended with a mucoid, slightly turbid fluid. The bone-marrow was hyperplastic. No other gross lesions were present. *Streptococcus viridans* was recovered from the fluid of the joints and from the local implantation in the peritoneal cavity. Cultures from urine, bile, blood and peritoneal fluid and from the substance of the bone-marrow, spleen, kidney and liver remained sterile.

D 39 was killed and examined twenty-four days following inoculation. The joints had returned to normal, showing no visible changes. The wall of the entire left ventricle (fig. 1) was diffusely thickened, white and opaque. The tips of the papillary muscles were slightly scarred and contracted. The chordae tendineae were thickened. The margins of the mitral leaflets were irregularly thickened and contained grayish, translucent nodules, from 1 mm. to 3 mm. in diameter. Such nodules were also present in the upper portion of the leaflets and irregularly throughout the entire lining of the left auricle. These tended to occur in groups of from three to ten, near together. The surface of one such group had a thin coating of red, thrombotic material which was firmly adherent to the nodules. The surfaces of all the other

nodules were smooth. No ulcerations or soft friable vegetations were present. One cluster of nodules was present near the margin of the tricuspid valve. The myocardium contained a few scattered, gray flecks which were barely visible without magnification. The lungs contained many irregular areas of congestion, which were somewhat firm as if partially consolidated. The kidneys were swollen and rather soft. The cortex was pale and grayish. The urine contained albumin. No visible changes were present in other structures. *Streptococcus viridans* was recovered from the thrombotic nodule in the endocardium

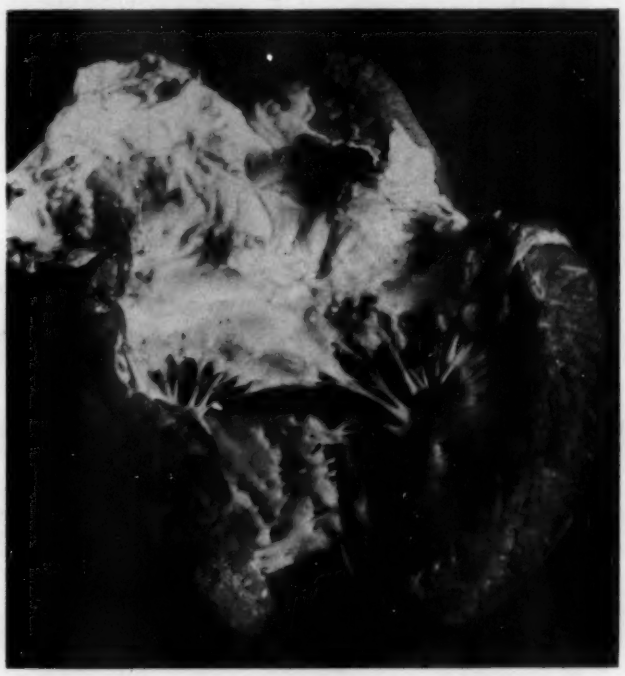


Fig. 1.—Heart of D 39, showing widely distributed verrucose endocarditis of the mitral and auricular endocardium and thickening of the mitral valve, of the chordae tendineae and of the papillary muscles. There is slight visible fibrosis of the myocardium.

and from the peritoneal implantation. It was not recovered from the blood, urine, bile, peritoneal fluid or joint fluid nor from the substance of the spleen, liver or kidneys.

D 38 was killed and examined twelve weeks after inoculation. The joints had returned to normal without visible change. The lining of the left ventricle and auricle was diffusely thickened and white. There were scattered pearly white nodules, from 1 to 2 mm. in diameter, along the margins of the mitral leaflets. No gross significant changes

were found in other structures. *Streptococcus viridans* was recovered from the peritoneal implantation. Cultures from the blood, bile, urine and peritoneal fluid and from the substance of the spleen, liver and kidneys gave negative results.

D 40 was observed during a period of twenty weeks, in the course of which five intravenous and peritoneal reinoculations with the same strain of *Streptococcus* had been made at intervals of from three to four weeks. There was evident stiffness with limitation of motion in the vertebral joints of the lumbar region and of the hips. This dog was inactive and lay quietly much of the time. Otherwise it appeared normal.

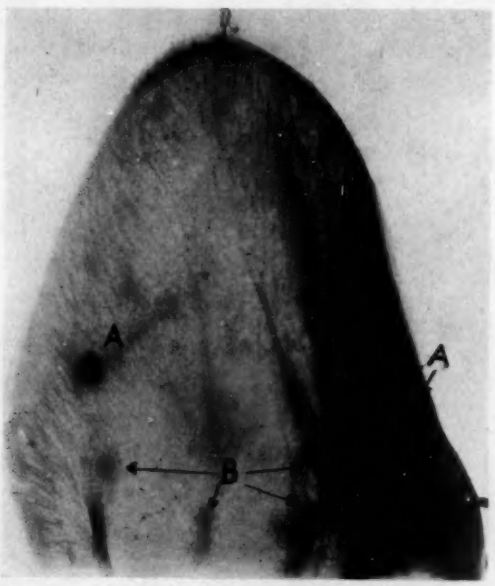


Fig. 2.—Ear of R 97, showing subcutaneous fibroid nodules at *A*, and small discolored areas at *B*, which are lesions healing without the formation of nodules. This photograph was made by transillumination; the opaque areas are rendered dark.

At postmortem examination the lining of the left auricle and ventricle was diffusely white and moderately thickened. Both the mitral and one of the tricuspid leaflets were scarred and thickened. An area, about 1 cm. in each diameter, in the tricuspid valve had a thickness of 2 mm. Along the free margin of the mitral leaflets there was a series of firm, gray, translucent nodules, ranging from 1 mm. to 3 mm. in diameter. The chordae tendineae were thickened, and the tips of the papillary muscles were slightly scarred and contracted. There was no apparent narrowing of the valvular orifices. The ventricular musculature con-

tained irregular gray flecks and patches, which appeared as scars. There were no gross visible changes in or about the joints. *Streptococcus viridans* was recovered in cultures from the peritoneal implantations only.

Arthritis developed within three days in three of the four rabbits inoculated. The temperature became elevated from 1 to 3 degrees. The leukocyte count ranged from 14,000 to 19,000. The rabbits became ill, ate little and lost flesh rapidly. The loss in weight ranged from 10 per cent to 25 per cent. Numerous red spots, about 2 mm. in diameter, appeared in the skin of the ears in three of them. Most of these spots faded after a few days and gradually disappeared. The others persisted, grew somewhat larger and formed firm, fibrous nodules

TABLE 1.—*Summary of Features Observed in Rabbits* *

Observations	R 96	R 97	R 98	R 99
Days elapsed after inoculation	28	11	4	9
Macroscopic observations				
Effusion into joints	+	+	—	+
Pericardial effusion	+	+	—	—
Subcutaneous nodules	+	+	—	+
Granular mitral vegetations	+	—	+	—
Visible myocardial streaks	+	+	+	—
Visible streaks in skeletal muscle	—	+	+	+
Weight when inoculated, Gm.	1,000	1,100	1,050	875
Weight at autopsy, Gm.	900	860		675
Microscopic observations				
Submaxillary nodules in myocardium	+	+	+	—
Pulmonary arterial lesions	+	+	—	—

* The signs + and — indicate the presence or absence, respectively, of the items specified.

about 5 mm. in diameter (fig. 2). *Streptococcus viridans* was recovered in cultures from these nodules during life.

One rabbit, R 99, died nine days following inoculation. The others were killed four days, eleven days and twenty-eight days after inoculation respectively. In three there was mucoid or mucopurulent effusion in the joints. *Streptococcus viridans* was recovered in cultures from the joints of two. Two had firm, granular, thrombotic vegetations on the mitral valve. In two there was marked pericardial effusion. This was serous. No fibrin and no adhesions were present. Cultures from the effusion remained sterile. In three there were firm subcutaneous nodules about the ears. In the heart muscle of three were scattered yellowish or grayish nodules about 1 by 3 mm. in size. These were elongated parallel with the muscle fibers and were firm. In three there were similar lesions in the skeletal muscles, involving principally the

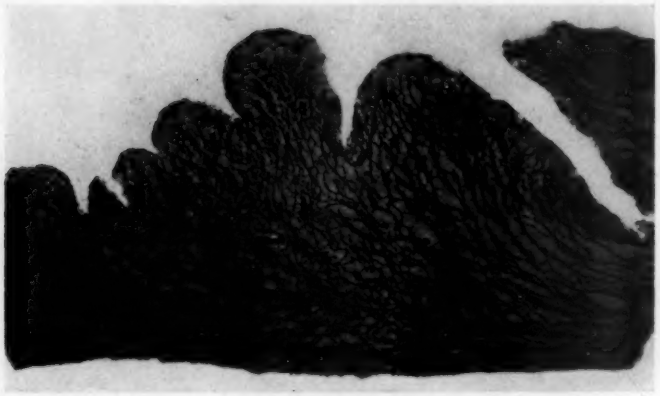


Fig. 3.—Small verrucose or granular vegetations from the auricular lining of D 39 (fig. 1). These consist of loose connective tissue containing many vascular channels; × 100.

Fig. 4.—Small granular vegetation from the mitral valve of R 96. A thin coating of firm thrombotic material covered some of these nodules; × 100.

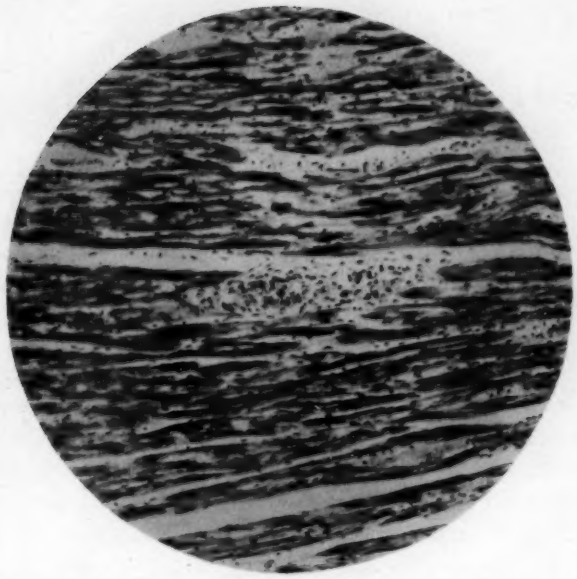


Fig. 5.—Myocardium of D 39, showing slight edema between the muscle fibers and a localized proliferative inflammatory lesion; × 100.

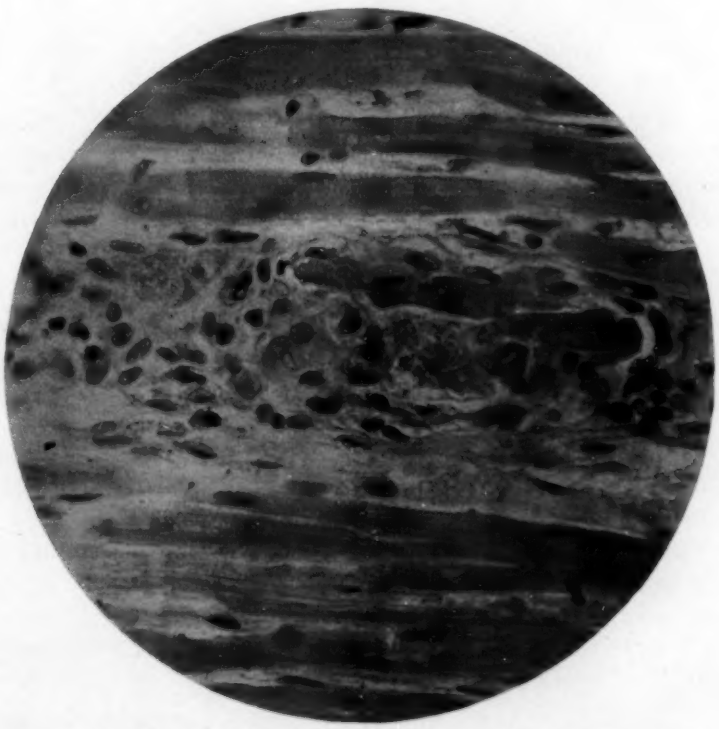


Fig. 6.—The same lesions as shown in figure 5; × 400. A few necrotic muscle fibers are surrounded by monocytes, some of which have two or three nuclei, plasma cells and fibroblasts.

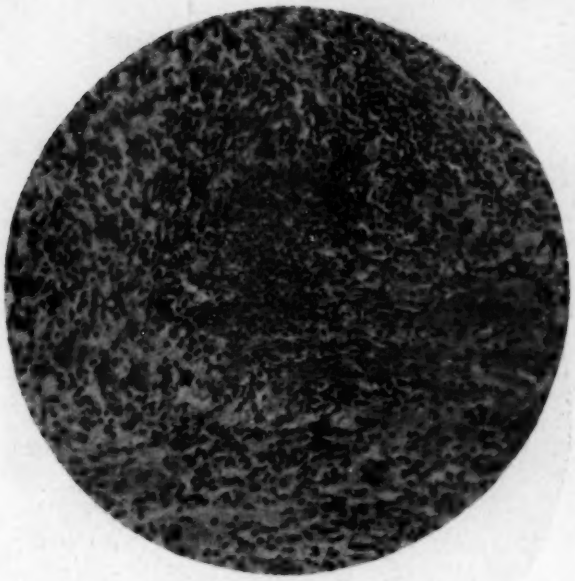
psoas, gluteal and lateral abdominal muscles. *Streptococcus viridans* was recovered in cultures from these lesions in the myocardium and skeletal muscles. No visible infarctions were present in any of the organs.

HISTOLOGIC FEATURES OF LESIONS

Small, translucent, gray nodules were present along the free margins of the mitral valves of D 39, D 40 and D 41. In D 39 these were present also in the auricular endocardium and on the tricuspid valve. Microscopically, these consisted of rather loosely arranged fibrous tissue and fibroblasts, forming rounded, villous or polypoid projections, covered by intact endothelium (fig. 3). These nodules contained small numbers of lymphocytes and monocytes, numerous capillaries and a few larger vascular channels. No thrombotic material was present on or about them. No bacteria could be demonstrated in sections stained by Gram's method. A small bit of firm thrombotic material was adherent to the mitral valve of R 96 (fig. 4). In this thrombus and in the nodule beneath it diplococci could be seen plainly in sections stained by Gram's method. Similar nodules were present in the mitral valve of R 98. These lesions were identical in structure with those found along the mitral margins in rheumatic endocarditis occurring in man.

Small localized lesions were found in the myocardium of D 39, R 96, R 97 and R 98. In D 39 these were few and occurred as small accumulations of monocytes, some of which had several nuclei, fibroblasts and lymphocytes, surrounding necrotic muscle fibers. They were not found in any characteristic relationship to arterial structures. In the spaces between muscle fibers throughout the sections there were small accumulations of similar cells (figs. 5 and 6).

In R 96, R 97 and R 98 the local lesions in the myocardium were numerous, and in most instances were situated adjacent to or surrounding small arterial branches. In R 98, killed four days after inoculation, the lesions consisted of a number of necrotic muscle fibers surrounded and infiltrated by polymorphonuclear leukocytes, eosinphils and mononuclear cells (fig. 7 *A*). In R 97, killed eleven days after inoculation, the larger nodules consisted of remnants of muscle fibers, surrounded by fibrous tissue containing many giant cells, monocytes and a few lymphocytes. The giant cells had homogeneous, slightly basophilic cytoplasm and had from four to twelve pale, oval nuclei. The smaller nodules occurred surrounding or adjacent to arterial twigs. Occasionally the arterial wall itself was involved. The giant cells here were larger. Their cytoplasm extended into the adjoining spaces between cells. There were more numerous fibrous tissue cells and fewer lymphocytes (fig. 8 *A* and *B*). Occasionally calcification was present in these



A

B

Fig. 7.—*A*, an early stage of a submiliary lesion in the ventricular wall of R 98. A number of necrotic muscle fibers are surrounded and infiltrated by monocytes, lymphocytes and plasma cells. Giant cells are beginning to form. A few leukocytes are present; × 200.

B, a submiliary lesion in the ventricular wall of R 97. This nodule is in a stage more advanced than that in *A*. An arterial branch is present adjacent to this nodule just outside the field to the left. Degenerated muscle fibers are seen at the right and at the left below the center. The black masses are calcified material; × 200.

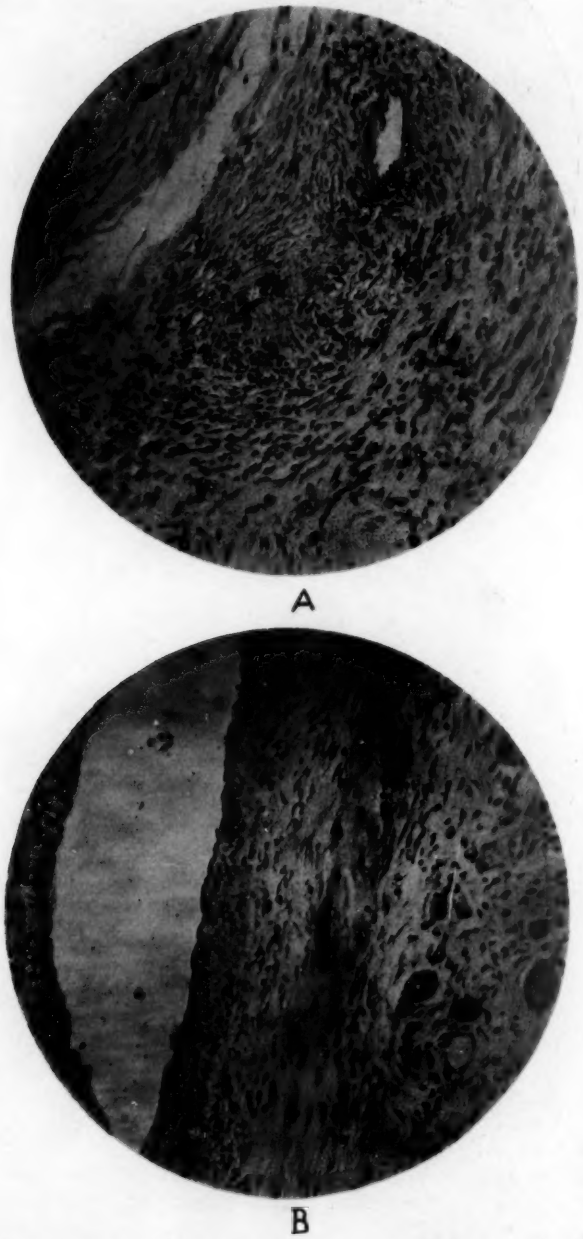
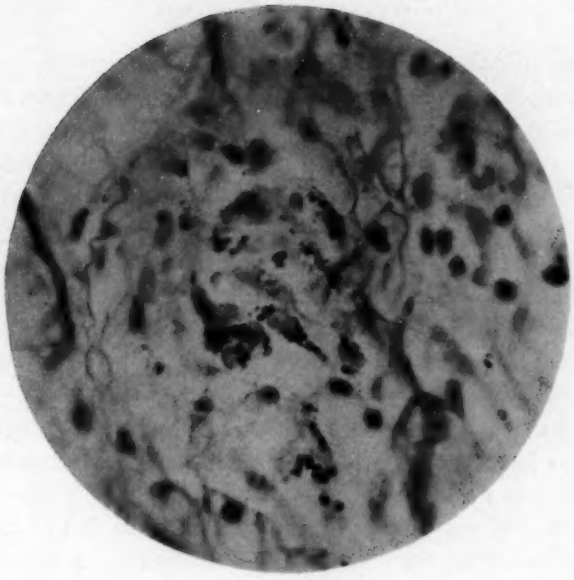
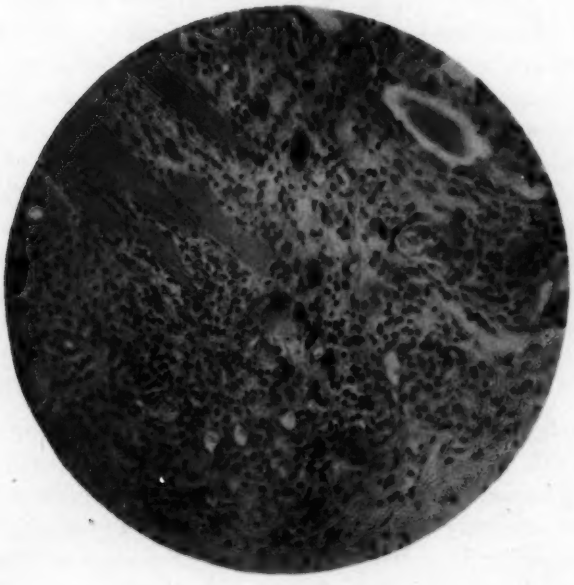


Fig. 8.—*A*, a smaller lesion than that shown in figure 7*B*. This lesion involves the wall of the adjacent arteriole. Ventricular wall of R 97; × 200. *B*, a small lesion, containing many giant cells, separated from an arterial wall by a few muscle fibers; × 200.



A



B

Fig. 9.—*A*, a section from the ventricular wall of R 97, stained by Gram's method and magnified 1,000 times. The monocytes and giant cells in a submiliary nodule contain many cocci in pairs, short chains and irregular clumps. Some are seen outside of cells.

B, the margin of a nodular lesion in the psoas muscle of R 99. Necrotic muscle fibers are surrounded by monocytes, small mononuclears and immature fibrous tissue cells. Many giant cells and vascular channels are present; × 200.

lesions. The submiliary nodules in the heart muscle of the rabbits were much larger than those in D 39. They varied from 0.1 mm. to 1 mm. in width and from 0.2 mm. to 1.5 mm. in length. Numerous cocci in pairs and clumps were demonstrable in some of these nodules (fig. 9 *A*). In those in which fibrosis was well marked, no bacteria could be seen. These nodules presented all the various features that characterize the Aschoff nodule (Clawson [3]).

The lesions in the skeletal muscles of R 97, R 98 and R 99 were larger than those found in the myocardium and appeared to have no relationship to the arteries. Otherwise their structure resembled that of the nodules found in the heart (fig. 9 *B*).

The auricular endocardium of D 39 and D 41 was increased to four or five times its normal thickness. This increase consisted of fibrous tissue which was distinctly hyaline. Beneath it were numerous whorls of fibrous tissue, submiliary in size, which caused the lining to be elevated. This gave the auricular endocardium a coarsely granular appearance readily seen in the photograph (fig. 1). Grossly these had a yellow color. Some of the nodules were markedly calcified. In others the deposit of calcium was slight. These granules in the endocardium were particularly numerous just above the root of the anterior mitral leaflet and in the auricular appendage. Von Glahn [4] described similar auricular lesions as a prominent feature in rheumatic hearts. He found such auricular involvement in nine of thirty-one cases of rheumatic endocarditis. He stated that the calcification was superficial, with the altered endocardium lying beneath it. In the dog's heart showing this feature, the calcium was deposited in fibrous nodules resembling healed submiliary lesions, lying beneath the thickened endocardium. We were unable to demonstrate micro-organisms in sections of the valvular or auricular lesions or in nodules in the myocardium from either of the dogs.

The small arteries in both dogs and rabbits and the aorta in one of the dogs, D 38, showed the type of changes which have been described [5] as occurring in rheumatic disease. In the intima and inner portion of the media of the coronary branches in D 39 there was marked proliferation of tissue, resulting in partial obstruction of the lumen. There was no apparent proliferation of the endothelium in these vessels. In D 38 the vasa vasorum of the aorta were surrounded by small accumulations

---

3. Clawson (footnote 1, second reference).

4. Von Glahn, W. C.: Am. J. Path. **2**:1, 1926.

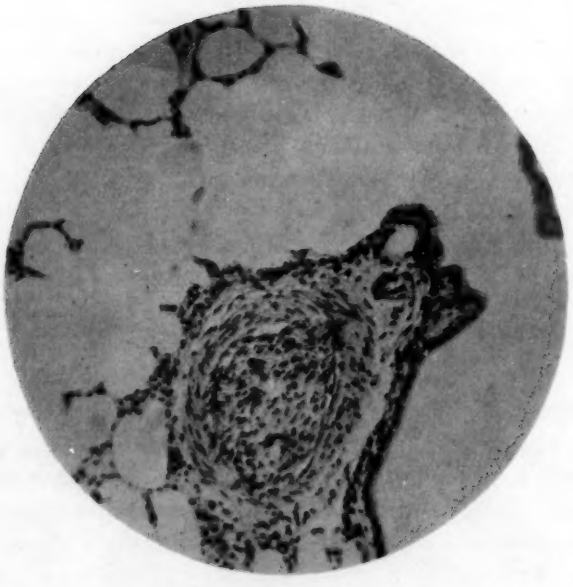
5. Klotz, O.: Tr. A. Am. Physicians **27**:183, 1912. Pappenheimer, A. M., and Von Glahn, W. C.: J. M. Research **44**:489, 1924; Am. J. Path. **2**:235, 1926. Paul, J. R.: Medicine **7**:383, 1928.

of monocytes and lymphocytes. In the media there were local accumulations of large monocytes lying between the fibers. Presumably the pressure of the fibers caused the cells to be arranged in thin, flat layers, which in sections appear as rows, as suggested by Pappenheimer and Von Glahn.[5] There were occasional wedge-shaped fibrous nodules containing large mononuclear cells about the nutrient vessels in the outer margin of the media. In D 40 the vasa vasorum of the ascending aorta were abnormally large and numerous and were conspicuous even in the inner portion of the media. This feature was first described by Klotz.[6] There were small local areas in the media where the muscular and elastic tissue had disappeared and had been replaced by delicate scars. Nothing resembling Aschoff nodules was seen in this aorta.

The smaller arteries, especially in the lungs, occasionally in the liver, spleen and kidney, showed proliferation of the endothelium, sometimes with narrowing of the lumen; in others, the lumen was completely obstructed. Frequently there were small, irregular vascular channels in the proliferation that filled the lumen. In no case was there evidence of thrombosis. In R 96 and R 99 and in D 38 and D 39 the pulmonary arterioles were markedly involved by proliferation of the endothelium. In R 96 approximately 75 per cent of the arterioles, the diameter of which was not larger than that of a normal renal glomerulus, were involved, as shown in fig. 10 *B*. In the alveolar walls were numerous small clumps of densely staining cells with oblong nuclei resembling endothelial cells. We are strongly of the opinion that these represented obliterated capillaries, but since no lumen was demonstrable this could not be verified. A similar change was present in the minute arterioles, the walls of which made identification possible. The alveolar septums adjacent to these clumps were distinctly thickened by fibrous proliferation. In some of the arterioles a definite infiltration of polymorphonuclear and lymphocytic cells was present both within and about the vessel. These were rather numerous in the lung and liver of D 39.

The subcutaneous nodules in the ears of R 99, which was killed nine days after inoculation, each consisted of a necrotic center containing numerous granules from nuclear destruction. Many polymorphonuclear and mononuclear cells were present in and surrounding the necrotic focus. No "palisade arrangement," frequently seen in rheumatic nodules in man, was present. In R 96, killed twenty-eight days after inoculation, these nodules consisted of a ground substance of hyaline material. Surrounding these hyaline areas and between them there was a proliferation of fibrous tissue cells of irregular shape, with no definite arrangement. No leukocytes or mononuclear cells were present. These nodules apparently were well advanced toward healing.

A



B

Fig. 10.— *A*, endarteritis with irregular thickening of the wall and narrowing of the lumen. Ventricular wall D 39; × 200. *B*, proliferative endarteritis in a branch of the pulmonary artery of R 96; × 200.

In the lesions seen in these dogs and rabbits there was no tendency to suppuration even where necrosis was marked. Uniformly the lesions were characterized by the presence of large and small mononuclear cells, giant cells and the formation of fibrous tissue.

LOSS OF VIRULENCE

A culture of the same strain used in the experiments had been kept in laboratory mediums for five weeks. During this time it had been transplanted repeatedly. After twenty-four hours at 37.5 C. the cultures had been held in refrigeration at about 4 C. It was noted that the character of the growth, both in broth and on agar, was modified. The colonies on agar were no longer firm and discrete, but were soft and

TABLE 2.—*Summary of Observations in Rabbits Inoculated with Growth of Low Virulence*

Features Noted	R 129	R 130	R 131	R 132
Tenderness of joints	—	+	—	+
Effusion in joints at autopsy	—	—	—	—
Pericardial effusion	—	—	—	—
Subcutaneous nodules	—	—	—	—
Granular mitral vegetations	—	+	—	—
Myocardial streaks	—	—	—	—
Streaks in skeletal muscles	—	—	—	—
Submiliary nodules in myocardium	—	—	—	—
Pulmonary arterial lesions	+	—	—	—

spread readily when touched. In broth the organisms no longer held together in firm masses, but grew in chains, producing turbidity with slight flocculation. The characteristic hemolysis and green discoloration on blood agar remained unchanged. Four young rabbits, weighing about 900 Gm. each, were inoculated in exactly the same manner as the first group described. The joints of two became slightly tender. No swelling was noticeable, and the joints returned to normal within forty-eight hours. The animals lost weight gradually and became anemic. The observations are summarized in table 2.

The organism inoculated was recovered in cultures from the chronic focus in three of these rabbits. In the case of one rabbit, which died some hours before examination was made, postmortem contamination made cultures unsatisfactory. The difference in the manifestations and in the gross and microscopic lesions in these two groups of rabbits was striking. Evidently the pathogenicity of this strain of streptococci was markedly changed by being held for a few weeks in artificial mediums.

SUMMARY

Young dogs and rabbits, not subjected to sensitization or other previous treatment, were inoculated with *Streptococcus viridans* from a case of bacterial endocarditis in man. The manifestations of disease which followed were very similar to the clinical features of acute rheumatic fever.

The gross and microscopic lesions in these animals were identical with those that characterize rheumatic disease. These lesions included verrucose valvular endocarditis, auricular endocarditis with calcification, rheumatic nodules—Aschoff bodies—in the myocardium, lesions of the rheumatic type in the aortic walls, proliferative endarteritis involving small arteries and fibroid nodules in subcutaneous and muscular tissues. Pericarditis with effusion was produced, but no pericardial adhesions.

The organism inoculated was recultivated from some of the lesions and was demonstrated microscopically in sections from others.

These results followed a combination of intravenous inoculation with implantation of chronic focus. It is not maintained that this mode of inoculation was essential to the production of the lesions. We believe the use of young animals and of freshly isolated cultures was of great importance in producing the lesions described.

CONCLUSION

The characteristic lesions of rheumatism can be produced by streptococci. The results obtained strengthen the evidence that streptococci of low virulence are the direct cause of rheumatic disease.

FIBROUS OSTEODYSTROPHY (OSTEITIS FIBROSA) IN EXPERIMENTAL HYPERPARATHYROIDISM OF GUINEA-PIGS *

HENRY L. JAFFE, M.D.

AARON BODANSKY, Ph.D.

AND

JOHN E. BLAIR, Ph.D.

NEW YORK

In another report,[1] the production of osteitis fibrosa as a result of experimental hyperparathyroidism in dogs was described. Also, the previous experimental attempts to produce this fibrous osteodystrophy and instances of its spontaneous occurrence in dogs, pigs, monkeys, cattle and horses were reviewed.

We decided to study the effects of parathyroid extract (parathormone Collip) on the bones of guinea-pigs, since the guinea-pig had been reported to be "immune" to the action of parathormone.[2] This conclusion was based on the absence of effect on serum calcium following the injection of parathormone. Our experiments on the effects of parathormone on the serum calcium and phosphorus of guinea-pigs failed to corroborate these observations.[3] With large doses of parathormone we obtained consistent effects on the serum calcium of guinea-pigs, and found that these effects could be brought out more prominently in young animals after prolonged fasting. In addition, changes in the bones were found, particularly in young guinea-pigs, whether hypercalcemia had been found or not.[4] The histologic changes produced in the tissues of the guinea-pigs, especially in the bones, following the injection of parathormone, will be described in detail, and the relation of these changes to nonexperimental osteitis fibrosa of lower animals and man will be indicated. The chemical observations will be touched on briefly. They have been reported elsewhere in greater detail.[3]

---

* Submitted for publication, July 21, 1930.

* From the Laboratory Division, Hospital for Joint Diseases.

* Eli Lilly & Company supplied some of the parathormone used in the experiments.

1. Jaffe, H. L., and Bodansky, A.: J. Exper. Med. **52**:669, 1930.

2. Macleod, J. J. R., and Taylor, N. B.: Tr. Roy. Soc. Canada (Sect. V. Biol. Sc.) **19**:27, 1926. Taylor, N. B.: Am. J. Physiol. **76**:221, 1926.

3. Bodansky, A.; Blair, J. E., and Jaffe, H. L.: J. Biol. Chem. **88**:669, 1930.

4. Jaffe, H. L.; Bodansky, A., and Blair, J. E.: Proc. Soc. Exper. Biol. & Med. **27**:710, 1930.

THE SPONTANEOUS OCCURRENCE OF OSTEITIS FIBROSA IN RODENTS

Lévy [5] described an adult tuberculous rabbit in which at autopsy metastatic calcification of the soft tissues was discovered. This led to histologic examination of the bones, which in the gross appeared normal in form and structure. Microscopically, generalized lesions of the bones were discovered, which were most marked in the tibia. There was extensive resorption with enlargement of the canals of blood vessels, resulting in thinning of the cortex. Replacement of the bone by connective tissue was observed in the enlarged canals of the blood vessels and on the surfaces of the cortex, where Howship's lacunae and osteoclasts were present. There was practically no formation of osteoid tissue, and few osteoblasts were observed. The metastatic calcifications were found in the kidneys, lungs, mucosa of the stomach and arterial walls. Lévy did not designate by name the condition that he described, but Christeller,[6] who restudied material from this case, was inclined to consider it one of acute progressive atrophy of bone, similar to that described by Askanazy in man.[7] He based his opinion on the fact that osteoblasts and osteoid tissue were practically absent in the greatly fibrosed bone. Because of the rarity of spontaneous fibrous diseases of bone in rabbits, it would be impossible to come to a decision as to whether Lévy's case was one of osteitis fibrosa or one of progressive atrophy of bone, or whether one is a stage of the other. Our experimental results on guinea-pigs indicate that Lévy had a case of true generalized osteitis fibrosa (see comment).

Pick [8] described a hedgehog, the skeleton of which showed nothing unusual macroscopically. On microscopic examination the bones showed terrific lacunar resorption by osteoclasts, and both the compact and the spongy bone were vascularized, and the enlarged canals of the blood vessels contained connective tissue. Fibrosis of the marrow was also present. The soft tissues showed metastatic calcification. Pick, as others before him, interpreted the metastatic calcification as an indicator of rapid and extensive resorption of bone. He believed that the changes observed in his animal were similar to those described by Askanazy in man and by Lévy in the rabbit, and that his and Lévy's cases represented early stages of osteitis fibrosa, modified in appearance because of differences of the species and somewhat different from the usual cases of osteitis fibrosa in man.

---

5. Lévy, E.: Arb. a. d. Geb. d. Path. u. Bakteriol. a. d. path. Inst. Tübingen **6**(pt. 2):555, 1908.

6. Christeller, E.: Ergebn. d. allg. Path. **20** (pt. 2):1, 1923.

7. Askanazy, M.: Beiträge zur Knochenpathologie, Festschr. f. M. Jaffé, Braunschweig, F. Vieweg & Sohn, 1901.

8. Pick, L.: Berl. klin. Wchnschr. **54**:797, 1917.

Pick also agreed with the further point that in lower animals and in man osteitis fibrosa may be diagnosed when there is intensive resorption of bone and fibrosis of the marrow, even without the presence of osteoid tissue. This statement is particularly applicable to lower animals.

THE PARATHYROID GLANDS AND MINERAL METABOLISM

Parathyroid hypersecretion (simple hyperplasia or benign adenoma) has been suggested as the cause of certain clinical dystrophies of bone. It is also known that the injection of parathormone into the dog [9] and man [10] leads to hypercalcemia and to increased excretion of calcium and phosphorus, particularly in the urine, and to lowered serum phosphorus and hypotonicity. The phenomena of overdosage in the dog have also been described—vomiting, diarrhea, hematuria, hemorrhagic gastro-enteritis, impairment of the kidneys, hyperphosphatemia and extensive metastatic calcification in the soft tissues, especially in the kidneys, heart, lungs and gastro-intestinal tract.[11]

It has also been established that in mice, rats and rabbits, relatively small, if any, effects on serum calcium are produced by the administration of relatively large doses of parathormone. These reports have been reviewed by us in another paper.[3]

Negative results after massive injections of parathormone in guinea-pigs were reported by Macleod and Taylor and Taylor.[2] However, we have shown that in guinea-pigs consistent effects on serum calcium and phosphorus could be produced by large doses of parathormone, and that these effects could be brought out more prominently in young animals particularly after prolonged fasting.[3] We have also shown that with doses not sufficiently great to produce effects on serum calcium and phosphorus, mobilization and excretion of calcium could be inferred from the microscopic examination of the bones.[4]

It is interesting to note that although Bauer, Aub and Albright [12] injected parathormone into young experimental animals in sufficiently large doses and for sufficiently long periods to suggest the probability that they had produced changes in the bones, they did not study bones histologically. The necessity of subjecting bone to histologic examination has been urged by many pathologists and is emphasized by the cases reported by Lévy and Pick. The bones of their animals appeared normal in the gross, but histologically these were greatly diseased.

---

9. Collip, J. B.: Medicine **5**:1, 1926. Greenwald, I., and Gross, J.: J. Biol. Chem. **68**:325, 1926.

10. Hunter, D., and Aub, J. C.: Quart. J. Med. **20**:123, 1927.

11. Hueper, W.: Metastatic Calcifications in Organs of Dog After Injections of Parathyroid Extract, Arch. Path. **3**:14, 1927. Learner, A.: J. Lab. & Clin. Med. **14**:921, 1929. Collip (footnote 9).

12. Bauer, W.; Aub, J. C., and Albright, F.: J. Exper. Med. **49**:145, 1929.

METHODS

Nearly all the guinea-pigs used in these experiments were raised in the laboratory. They were kept under hygienic conditions. Their diet consisted of carrots, cabbage, hay and oats. Water was supplied to all animals ad libitum. This diet has been fed to all guinea-pigs in this laboratory, and on it they thrive and reproduce during all seasons of the year.

Some of the experimental animals were caused to fast for long periods (from sixty to seventy-two hours). The experimental animals were given subcutaneous injections of parathyroid extract (parathormone Collip). The serum calcium was determined by the Clark-Collip method and the serum phosphorus by the Benedict-Theis method. Nearly all of the experimental animals were killed to terminate the experiments, and were examined immediately thereafter.

The tissues were fixed either in neutral formaldehyde or Helly's solution. The bones that were fixed in formaldehyde were decalcified in Müller's fluid plus 5 per cent glacial acetic acid, while those fixed in Helly's solution were decalcified in 5 per cent nitric acid. Some of the soft tissues were fixed in 95 per cent alcohol and were stained for calcium by the von Kossá method. The tissues were embedded in paraffin and stained with hematoxylin and eosin.

Four types of experiments were done: (1) on the effects of large single doses of parathormone on young fed guinea-pigs and on young guinea-pigs that had fasted for various periods; (2) on the effects of large single doses of parathormone on adult fed and fasting guinea-pigs; (3) on the effects of repeated doses of parathormone on young guinea-pigs; (4) on the effects of intermittent treatment of young guinea-pigs with large doses of parathormone (with production of osteoid tissue).

In addition, the bones from nineteen untreated young and old, fed and fasting guinea-pigs were studied as controls for the treated guinea-pigs under the conditions of the experiments. Our experience of several years with the bones of guinea-pigs under a variety of experimental conditions served as an additional control in the interpretation of the changes in the bones. Resorption of bone, which is a prominent feature of these lesions, has been discussed by one of us.[13]

EFFECTS OF A LARGE SINGLE DOSE OF PARATHORMONE ON THE BONES

In Young Guinea-Pigs Fed to the Time They Were Killed.—Eleven guinea-pigs, each weighing between 280 and 368 Gm., were given a subcutaneous injection of 20 units of parathormone per hundred grams of body weight. They were killed at intervals of six, twelve, eighteen, twenty-four, thirty-six and forty-eight hours after the administration of parathormone.

At six hours, examination of the ribs showed slight congestion of the marrow in the vicinity of the costochondral junction, and definite, but slight, subperiosteal resorption, as indicated by the presence of a number of Howship's lacunae and osteoclasts on the shafts of the ribs. At twelve hours after the injection of parathormone, the ribs showed

13. Jaffe, H. L.: Am. J. Path. **5**:323, 1929; Resorption of Bone; Consideration of Underlying Processes, Particularly in Pathologic Conditions, Arch. Surg. **20**:355, 1930.

more advanced changes: subperiosteal resorption was more advanced, the lacunae containing osteoclasts; the canals of blood vessels of the compacta were enlarged, and the marrow had undergone some fibrous replacement at the costochondral junctions, where the new formation of endochondral bone showed signs of diminution. By the eighteenth hour, the changes had advanced further: Howship's lacunae beneath the periosteum of the shaft were now very deep and contained fibrous tissue and osteoclasts; underneath the endosteum was an attempt at formation of bone; the canals of blood vessels of the shafts of the ribs were enlarged and contained connective tissue; fibrous tissue replacement was observed in the marrow at the costochondral junction and was considerable in one of the animals; new endochondral ossification had ceased at the costochondral junction. Ribs from the guinea-pig killed twenty-four hours after the injection of parathormone showed changes of about the same degree. However, the ribs of an animal examined thirty-six hours after the administration of parathormone showed still more pronounced changes: the resorption of bone was extensive; subperiosteally, the cortex showed considerable excavation, deep Howship's lacunae with osteoclasts on their walls, and connective tissue; there was replacement of the lymphoid marrow by connective tissue, most marked at the costochondral junction, where it filled the marrow cavity and extended for a considerable distance immediately underneath the cortex. By the forty-eighth hour, even more extensive changes were observed: the cortex near the costochondral junctions was fractured, owing to severe decalcification; the rest of the shaft showed extensive resorption; the canals of blood vessels were much enlarged and contained fibrous tissue; there was very extensive hemorrhage and edema of the marrow at the costochondral junction, where the marrow was also fibrosed; formation of bone had ceased, particularly at the costochondral junction.

Young guinea-pigs, therefore, receiving a large single dose of parathormone, showed definite, but slight, histologic changes as early as the sixth hour after the administration of parathormone, which became progressively more intense to the forty-eighth hour, the longest interval of time employed. At this period decalcification was so marked that the cortices of the ribs were frequently fractured. Often the cortex near the costochondral junction was converted into a pink-staining tissue consisting of disorganized fibrils of bone, and the fibrils remained after removal of the inorganic constituents of the matrix. These results were striking evidence of the severe and extensive decalcification that one large dose of parathormone is capable of inducing in guinea-pigs. See figure 1.

Study of the serum calcium and phosphorus of these eleven animals showed a slight variation from the normal. The calcium tended to be

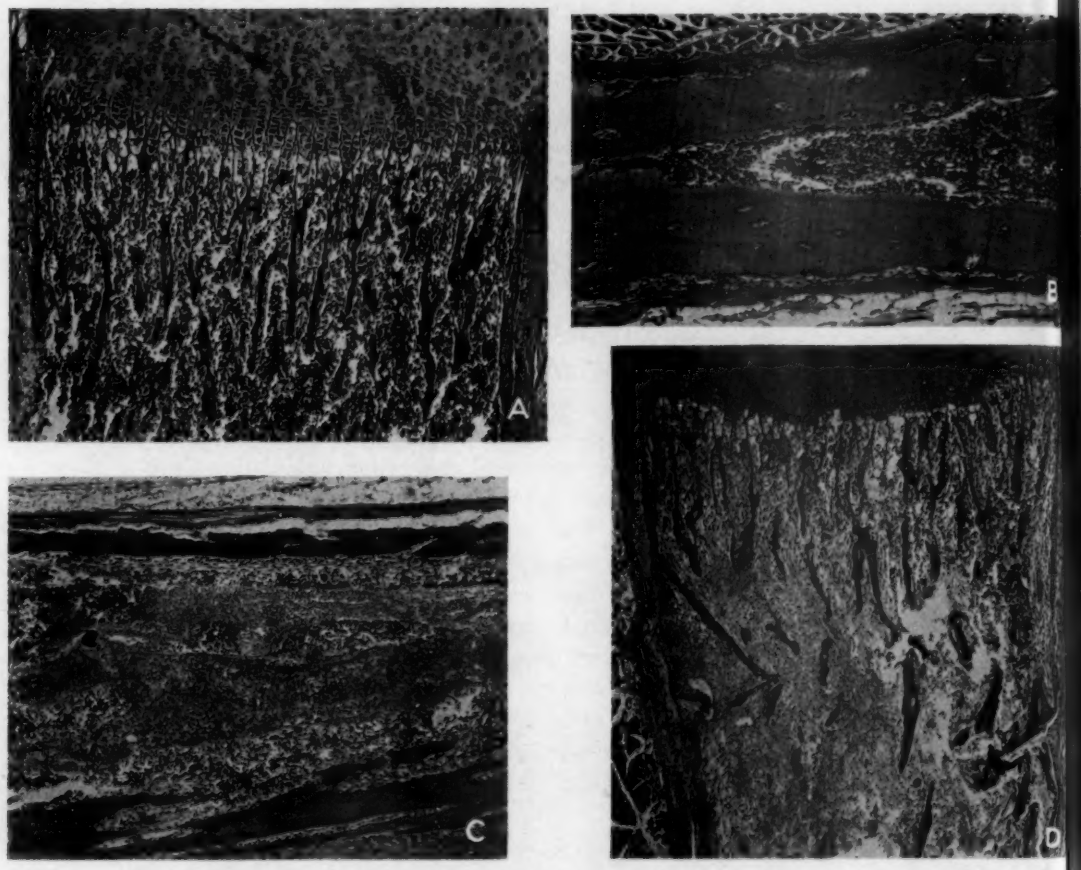


Fig. 1.—*A*, the costochondral junction of a rib of a young control guinea-pig weighting 280 Gm. The cartilage columns are regular, and endochondral ossification is active; the lymphoid marrow extends to the costochondral junction. Magnification, × 60. *B*, the shaft of the rib shown in *A*. The cortex is compact; the canals of the blood vessels are small; lymphoid marrow occupies the medullary cavity. Magnification, × 60. *C*, the shaft of the rib of a young guinea-pig weighing 300 Gm. The animal was killed forty-eight hours after the injection of 60 units of parathormone, and had been permitted to feed. The lymphoid marrow has disappeared, and the marrow cavity is filled with blood, the result of free hemorrhage. The cortex already shows extensive resorption and enlargement of the canals of blood vessels. These canals contain fibrous tissue. Magnification, × 65. *D*, the costochondral junction of the rib shown in *C*. The marrow is degenerated; the cortex is fractured in numerous places; the columns of endochondral bone are splintered, and new endochondral ossification has ceased. Magnification, × 65.

higher at twenty-four and thirty-six hours after injection. The serum phosphorus values showed a distribution not far above the zone of the values found for the fed controls.

The striking feature brought out in the study of these eleven guinea-pigs is that in spite of the progressively increasing intensity of the lesions of the bones over a period of forty-eight hours, there was relatively little change in the serum calcium and less in the serum phosphorus. It illustrates the difficulty of obtaining hypercalcemia in young guinea-pigs that are being fed. It shows that nevertheless there was a progressive effect of the parathormone, either directly or indirectly, on the bone and bone marrow, and that hyperparathyroidism existed. The results indicate that hypercalcemia should not be used as a sole criterion of hyperparathyroidism. The reasons for the absence of marked hypercalcemia may possibly be found, as we have indicated elsewhere, in an increased rate of the excretion of calcium, or possibly the hypercalcemia was counteracted by feeding, since the diet of our guinea-pigs yields in the course of metabolism a basic balance. It is known that parathyroid hypercalcemia may be decreased by bases.[14]

In Young Fasting Guinea-Pigs.—Six young guinea-pigs varying in weight from 310 to 360 Gm. were made to fast from sixty to seventy-two hours. At intervals of from three to forty-eight hours before the termination of the experiment, an injection of parathormone was given equivalent to 20 units per hundred grams of body weight. These animals also showed a progression of the pathologic changes, as observed in the ribs of the fed series, becoming more intense to the forty-eighth hour, which was the longest interval of time employed. At this period, decalcification was so marked that the cortex of the ribs was fractured. The cortex near the costochondral junction was converted into a pink-staining tissue, consisting of disorganized fibrils of bone, the fibrils remaining after removal of the organic constituents of the matrix. The changes after forty-eight hours were possibly slightly more severe in the fasting than in the fed animals, although an insufficient number of animals was studied to allow definite conclusions. It is observed, therefore, that changes in the bones after a single large dose of parathormone were of the same order and extent in fed and fasting animals.

The effects of prolonged fasting were, however, reflected in the figures for serum calcium and phosphorus. The results for these six animals, with those for seventeen additional animals the bones of which were not studied microscopically, showed an increase in the serum calcium as early as four hours after the injection, rising to a maximum after from eighteen to thirty-six hours and persisting at a high level to forty-eight hours after the injection. The serum phosphorus in these

14. Stewart, C. P., and Percival, G. H.: Biochem. J. **21**:301, 1927.

animals rose high above that of the fasting controls (not receiving parathormone), indicating overdosage.

Thus it is observed that prolonged fasting helped to demonstrate hypercalcemia, but the bone changes resulting from the hyperparathyroidism were observed in both fasting and fed animals, with and without hypercalcemia, respectively.

That prolonged fasting, as such, could not raise the serum calcium of the guinea-pig or induce the bone changes described was shown by an examination of six fasting young controls, the values of the serum calcium and phosphorus of which were normal; the bones of four of these animals showed, on histologic examination, only the usual effects of starvation on the bone marrow—that is, the opening of innumerable blood sinuses in the marrow. In addition there was diminution in the formation of new endochondral bone at the costochondral junctions. In none of the sections was there much enlargement of the canals of blood vessels, nor was there fibrous invasion of the marrow and bone. An abnormal number of osteoclasts and Howship's lacunae were not observed.

In Adult Guinea-Pigs Fed to the Time They Were Killed.—Six adult guinea-pigs, each weighing between 620 and 730 Gm., were given an injection of a single large dose of parathormone (20 units per hundred grams of body weight) twelve, twenty-four and forty-eight hours before they were killed. In no instance were marked effects observed in the bones, such as enlargement of the canals of blood vessels, subperiosteal and subendosteal resorption with osteoclasts in Howship's lacunae, or necrosis of marrow and fibrosis of bone and marrow. The serum calcium tended to rise and was definitely high at twenty-four hours. The serum phosphorus values were slightly above the normal range.

It is almost inconceivable that the large doses of parathormone injected into these adult guinea-pigs did not have some effect on their acid-base equilibrium, with some effects on the calcium reserves of the bone. We have found histologic examination useful in demonstrating the effects of parathormone in the bones of young guinea-pigs, in which we have been able to study the results of experimental hyperparathyroidism. We have observed identical changes in the bones of young guinea-pigs, dogs and rabbits given each a single large dose of parathormone. It is possible that in the adult guinea-pigs, while the histologic examination showed no obvious effects of experimental hyperparathyroidism, chemical analyses, which are capable of greater precision, would have shown slight quantitative differences in the treated adult, as compared with the control adult animals.

We doubt whether these adult guinea-pigs are immune to such large doses of parathormone. They showed definite effects on the serum calcium, and the serum phosphorus also seemed to be affected. We believe, however, that the effects of hyperparathyroidism on the bones may be qualitatively different in young and adult guinea-pigs. Much larger doses of parathormone might have induced severe changes in the bones of the adults. An important qualification in all discussions of the changes in the bones in experimental hyperparathyroidism is that they are most marked in the young animals, in the most actively growing portions of the bone, that is, at the costochondral junctions or in the subepiphyseal regions of the metaphysis or in the ends of the diaphyseal cortex. Clinical cases of osteitis fibrosa cystica, with parathyroid adenoma, likewise occur in young persons, in whom the lesions probably have been developing from infancy or childhood.[15] It seems that the physiologic state of the bone is important in eliciting the effects of hyperparathyroidism.

In Adult Fasting Guinea-Pigs.—Seven adult guinea-pigs, each weighing between 620 and 860 Gm., were studied. They were made to fast for seventy-two hours before they were killed, and were given an injection of a single large dose of parathormone (20 units per hundred grams of body weight) six, twelve, twenty-four and forty-eight hours before being killed. The bones of none of these animals showed resorption of bone or fibrosis of marrow, though two of them showed a slight increase in the number of subperiosteal and subendosteal osteoclasts, which may in itself have been due to fasting rather than to the parathormone. In these animals the effects on the serum calcium were slight and not much greater than in the fed guinea-pigs. The values of the serum phosphorus were generally slightly above the normal range.

In these doses, therefore, the hyperparathyroidism that was induced was associated with only slight elevation of the serum calcium and phosphorus, and there were no obvious effects on the bones on histologic examination.

EFFECTS OF REPEATED DOSES OF PARATHORMONE ON THE BONES

In Young Growing Guinea-Pigs.—As stated in our report of the chemical results,[3] the animals used in these experiments were all young; the initial weight of most of them was between 300 and 400 Gm.; a few weighed more, 470 Gm. being the weight of the heaviest. In order to observe the condition of the guinea-pigs during the progress of the experiments, they were weighed at frequent intervals. Five groups of experiments were carried out. Group 1 included five animals given daily injections of 10 and 20 units for ten and sixteen days. Group 2 included

15. Hirsch, I. S.: Radiology **12**:505, 1929; **13**:44, 1929.

two animals treated for thirty-four days; the maximum daily dose was 16 units, preceded in one of the guinea-pigs by previous treatment with smaller doses. Group 3 included animals given preliminary daily treatment with small doses, followed by large doses—up to 60 units. Group 4 consisted of animals receiving large daily doses for three days without preliminary treatment. Group 5 included animals receiving very large daily doses (from 60 to 100 units) for four days after preliminary treatment with smaller doses.

When receiving 10 units or less daily, the animal gained weight. On about 20 units in the short experiments, the weight generally rose. In our longest period, thirty-four days, with a daily dose of 16 units, the animals continued to gain until the twenty-third day, then lost relatively rapidly until the twenty-seventh day, after which their weights remained practically stationary. On larger doses, loss of appetite was indicated by stationary or slightly decreased weight, and when the large doses were continued, larger losses in weight occurred.

We noted the effects of the repeated doses of parathormone on the serum calcium and phosphorus. The guinea-pigs were bled usually at the end of the test, but in several cases also during the progress of the test, preferably just before a dose was increased. In view of our observations of the long persistence in guinea-pigs of the effect of a single injection of parathormone, the serum calcium and phosphorus at any time during the course of daily injections were assumed to be under the influence of the last two, or perhaps three, doses injected. The significance of the interval between the last injection and bleeding was therefore reduced.

Our guinea-pigs were bled less than twenty-four hours after removal of food, for we found that after a single injection of parathormone there were no marked differences between the values of the serum calcium and phosphorus of guinea-pigs fed to the time of bleeding and those of guinea-pigs that had fasted for twenty-four hours or less.

Group 1: 10 and 20 Units Daily for Ten and Sixteen Days.—One animal receiving 10 units of parathormone daily for ten days showed in the sections of the ribs slight subperiosteal resorption with some Howship's lacunae; there was very slight fibrosis of the marrow at the costochondral junction. Three guinea-pigs receiving 10 units daily for sixteen days showed to a great degree similar changes, the lighter animals showing the more severe lesions, because of the relatively larger dose. Sections of their ribs showed a generalized thinning of the cortex. Subperiosteally there was osteoclastic resorption, with Howship's lacunae. Some of the haversian canals of the cortex were enlarged and contained fibrous tissue. There were Howship's lacunae and osteoclasts on the walls. A few perforating canals were observed extending through the entire thickness of the cortex. The marrow was congested, the blood

sinuses were dilated, and a slight amount of free blood was present, with evidence of phagocytosis. The marrow was scarred, especially near the costochondral junction. In this area there was cessation of the formation of new bone, with evidence of osteoclastic resorption. In some of the ribs there was subperiosteal formation of callus. See figure 2.

One animal receiving 20 units daily for ten days showed essentially the same changes.

With these doses of parathormone, no clear effect on the serum calcium was obtained, the average value being within the normal range.

Group 2: Daily Treatment for Thirty-Four Days.—One of two animals received 2 units of parathormone daily for eight days, 8 units for seventeen days and 16 units daily for nine days. It showed definite

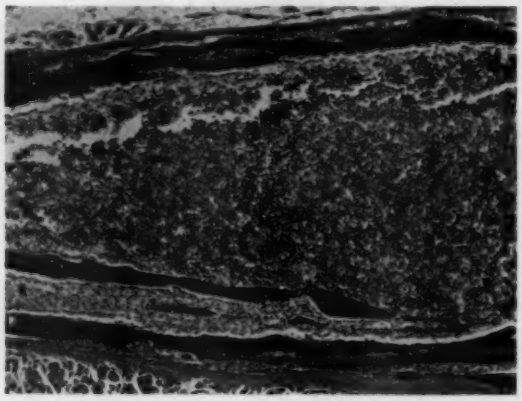


Fig. 2—The shaft of a rib of a guinea-pig weighing 260 Gm. when injection with 10 units of parathormone daily was begun. The animal was killed after sixteen days; at this time it weighed 323 Gm. The cortex is thin; there is marked subperiosteal resorption; the canals of blood vessels are enlarged and filled with vascular fibrous tissue; the marrow is congested, and some free hemorrhage is present. Magnification, × 65.

osteoclastic resorption of the cortex of the ribs and femur. The enlarged canals of blood vessels contained fibrous tissue, with some fibrosis of the marrow at the costochondral junction and at the metaphysis. The lesions were somewhat less severe than those observed in guinea-pigs receiving 20 units daily for ten days, the severity of the lesions having probably been modified by the previous preparation with the smaller doses and the greater weight of the animal. The serum calcium on the twenty-fourth day was normal (after seventeen days on 8 units); but on the thirty-fourth day, after nine days on 16 units daily, it was 16.7 mg. per hundred cubic centimeters. The serum phosphorus value at this time was apparently normal.

In the other animal, given 16 units daily for the entire thirty-four days, the ribs showed resorption. The canals of blood vessels were enlarged and contained fibrous connective tissue. The marrow at the costochondral junctions and at the metaphyses was fibrosed. The serum calcium was 12.1 mg. per hundred cubic centimeters after eight days, and 11.6 mg., on the thirty-fourth day. The serum phosphorus value was normal.

Group 3: Preliminary Daily Treatment With Small Doses, Followed by Large Doses, up to 60 Units on the Last Day.—Four guinea-pigs were given 5 units of parathormone daily for two days, 10 units for four days, 20 units for four days, 30 units for four days, 40 units for one day and 60 units for one day. Sections of the ribs and long bones showed pronounced resorption of cortical bone with marked enlargement of the canals of blood vessels, and the canals contained much connective tissue and osteoclasts. The marrow at the costochondral junctions and underneath the epiphyseal cartilage plates was scarred and contained numerous dilated blood sinuses, considerable free hemorrhage and osteoclasts. Formation of endochondral new bone at the epiphyseal cartilage plates and the costochondral junctions had ceased. The changes varied somewhat in degree with the individual animal, one of them showing more acute changes, with acute degeneration of the marrow. See figure 3.

Guinea-pigs showing a greater degree of reaction to the hyperparathyroidism presented edema of the subcutaneous tissues of the abdomen and wall of the chest. These edematous tissues contained numerous eosinophils and many neutrophil leukocytes. The fibers of the heart muscle were degenerated and fragmented in some and showed metastatic calcification. The spleen showed fibrosis. These four guinea-pigs were suffering from acute hyperparathyroidism, the results of which were reflected in both bones and soft tissues. The serum calcium was elevated above normal. The serum phosphorus values were within the normal range.

Group 4: Three Large Daily Doses Without Preliminary Treatment.—Three guinea-pigs, each weighing about 320 Gm., were given injections of 20, 40 and 60 units daily on three successive days. They all died during the third day, before the serum calcium could be determined. Their bones and soft tissues showed very severe effects. The ribs were extensively resorbed, the haversian canals being enlarged and containing much fibrous tissue and numerous osteoclasts. At the costochondral junctions there was extensive necrosis of the bone, with very rapid decalcification, resulting in pink-staining areas—masses of disorganized fibrils of bone, the remains of the organic matrix. There was some edema between the fibrils, and the tissue of the disorganized

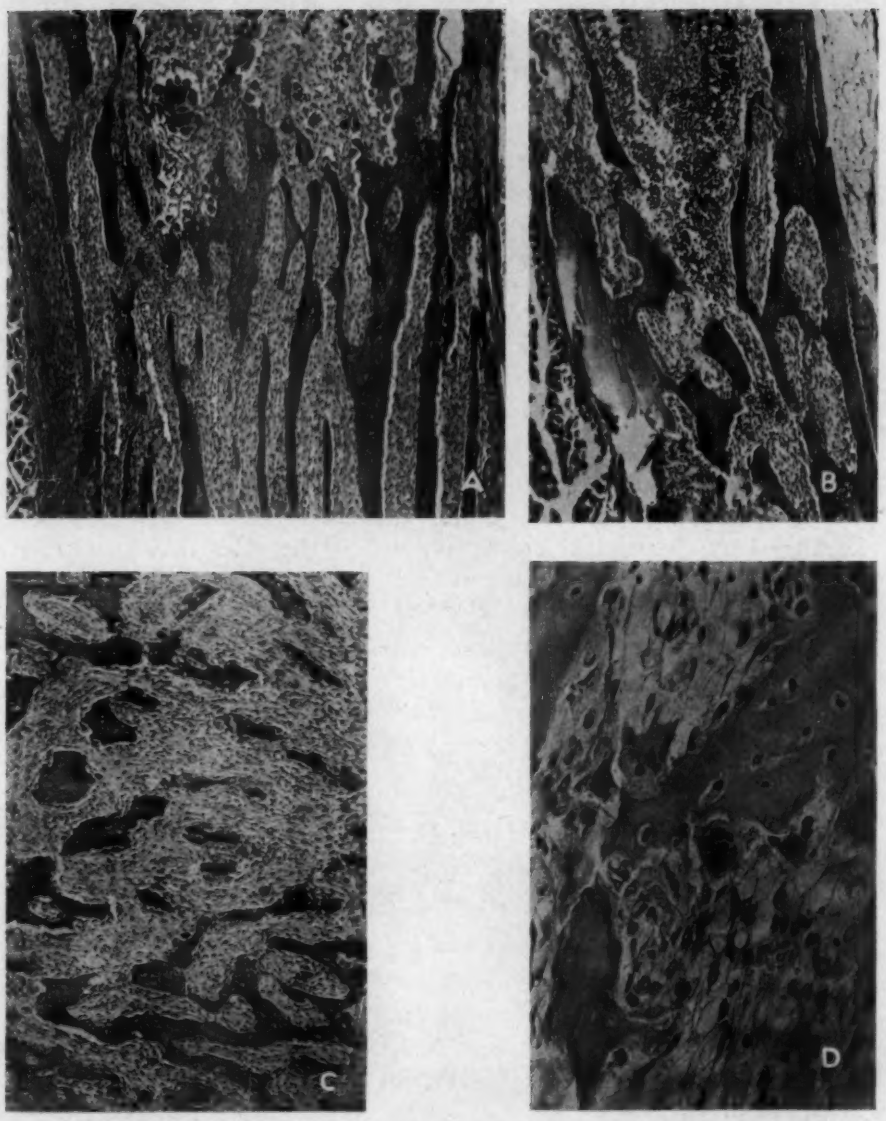


Fig. 3.—*A*, a section from near the costochondral junction of a rib of a guinea-pig weighing 276 Gm. The guinea-pig was given daily treatment with small doses followed by large doses, up to 60 units on the last day. It was killed sixteen days after the beginning of the experiment; at this time it weighed 356 Gm. The marrow is considerably scarred and contains numerous dilated blood sinuses and osteoclasts. The resorption of bone is pronounced, and the enlarged canals of blood vessels contain much fibrous tissue and osteoclasts in Howship's lacunae. Magnification, × 60. *B*, the shaft of the rib shown in *A*. Marked enlargement of the canals of blood vessels and numerous Howship's lacunae and osteoclasts are observed. Magnification, × 60. *C*, an area of metaphyseal fibrosis in a guinea-pig weighing 270 Gm. at the beginning of the experiment and treated like the animal from which *A* and *B* were taken. The guinea-pig weighed 315 Gm. when killed. Observe the marked fibrosis of the marrow and resorption of bone. Magnification, × 60. *D*, the details of the osteoclastic resorption of bone and of the fibrosis of the marrow shown in *C*. Magnification, × 360.

matrix had been rapidly vascularized. Formation of new bone had ceased at the costochondral junction, and the trabeculae of bone deposited on the cartilage cores had been dissolved. Throughout the marrow there were areas of necrosis. The necrotic marrow contained numerous neutrophil leukocytes. At the costochondral junction, the marrow was extremely vascularized, somewhat fibrosed and showed free hemorrhage. Fracture of some of the ribs occurred in this region. The changes in the long tubular bones were of the same order as those described in the ribs, and the severest changes in the marrow were found in the metaphyses. Where fractures had occurred in the bones, an attempt at repair by subperiosteal callus was already evident. See figure 4 *A, B* and *C*. The soft tissues in the kidneys, gastric mucosa, lungs and heart showed considerable metastatic calcification. The fibers of the heart muscle were degenerated and fragmented (figure 4 *D*). The subcutaneous tissues of the abdomen showed edema, necrosis and metastatic calcification. Some of the other organs and tissues were congested.

Two guinea-pigs, each weighing about 375 Gm., received 80 units daily for three days, and two received 40 units daily for three days. All died before the blood could be examined. The changes in the bones were as described in the preceding paragraph, but more severe, the necrosis of the marrow being more marked, with large cystic spaces appearing in the marrow at the costochondral junctions and in the metaphysis. See figure 5.

Group 5: Four Very Large Daily Doses (from 60 to 100 Units) after Preliminary Treatment with Smaller Doses.—This group showed many striking differences when compared with group 4. After from one to three weeks of preliminary treatment with small doses of parathormone (from 8 to 10 units), the doses were rapidly raised to 60 and even to 100 units daily and maintained at these high points for several days, without the guinea-pigs succumbing. By the end of the experiment, one such animal had been receiving 60 units a day for three days; another, 60 units for four days, and a third, 100 units for four days. The serum calcium was very high in these animals, being 16.9, 20 and 18.5 mg. per hundred cubic centimeters, respectively, at the termination of the experiment, but it is striking that no hyperphosphatemia developed, the serum phosphorus being 7.7, 6.6 and 6.9 mg. per hundred cubic centimeters.

The histologic examination of the bones confirmed the protective effect that is exercised by preliminary treatment with small doses of parathormone. The bones were resorbed, and the enlarged canals of blood vessels contained fibrous tissue, embedded in which were numerous eosinophils. The connective tissue contained numerous osteoclasts,

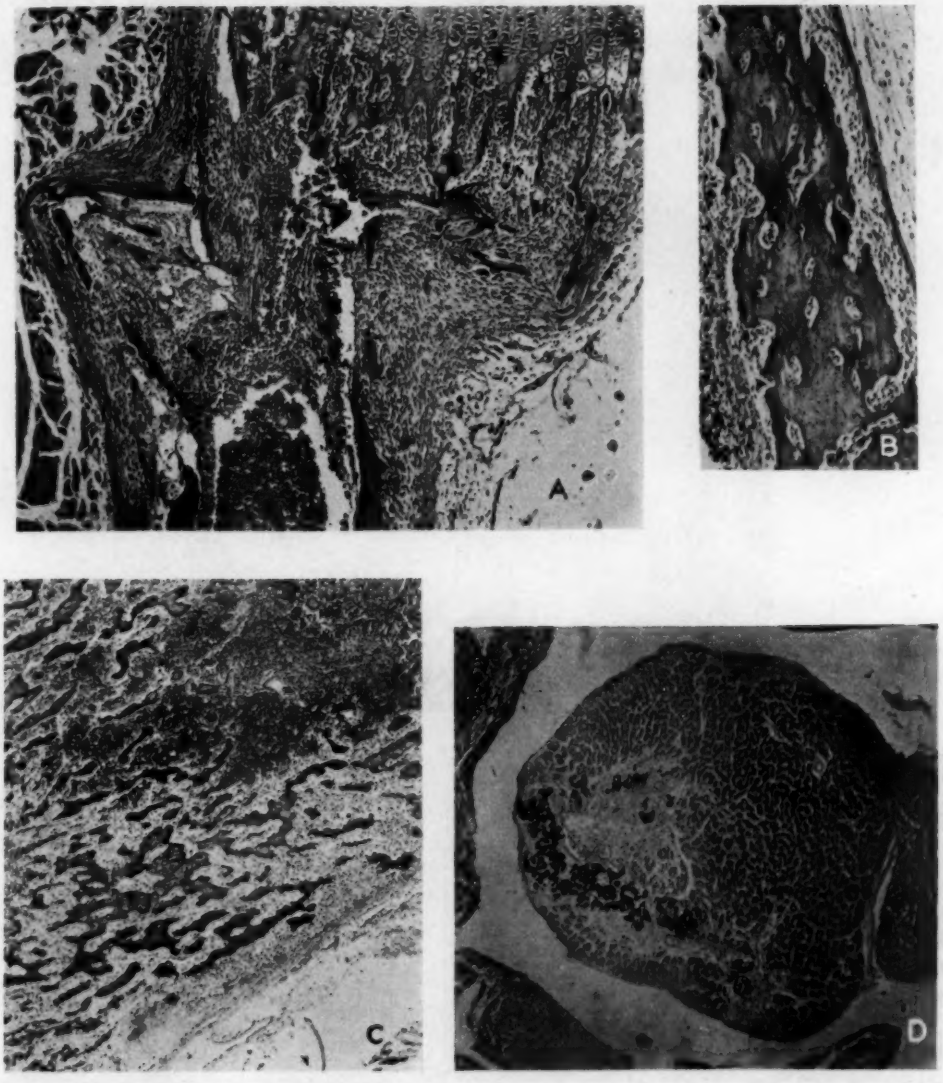


Fig. 4.—*A*, the costochondral junction of a rib of a guinea-pig weighing 300 Gm., given 20, 40 and 60 units of parathormone on three successive days. There is extensive necrosis of bone and rapid decalcification; fractures are present. Hemmorrhage of the marrow and fibrosis are observed. An attempt at subperiosteal repair is present. Magnification, × 60. *B*, cortical resorption of the shaft of a long tubular bone from the same animal as *A*. Magnification, × 60. *C*, shaft of a long tubular bone of a guinea-pig receiving three large doses of parathormone. Note the extensive resorption and fibrosis of the cortex. Magnification, × 20. *D*, the heart muscle of an animal given several large doses of parathormone; metastatic calcification is observed. Von Kossá stain is used. Magnification, × 60.

and the bone showed numerous Howship's lacunae. The marrow was fibrosed, especially at the costochondral junctions and in the metaphyses. The striking feature was the absence of acute degeneration of the marrow, which had been observed in all guinea-pigs given large doses without preliminary treatment.

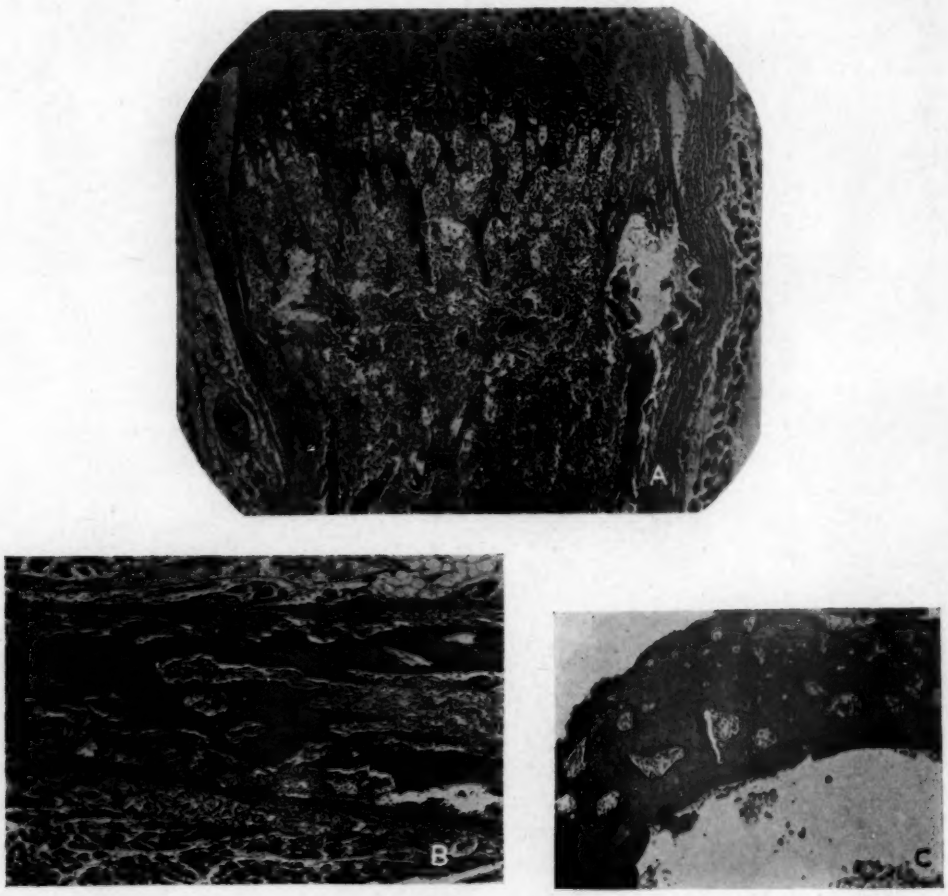


Fig. 5.—*A*, the costochondral junction of a rib of a guinea-pig weighing 375 Gm.; the animal had received 80 units of parathormone for three days. Acute decalcification is observed, with fractures of the cortex. There are degeneration and fibrosis of the marrow. Magnification, × 60. *B*, the shaft of the rib shown in *A*. Note the extensive resorption of the cortical bone and the fibrosis of the marrow. See *A*. Magnification, × 60. *C*, a section through the middle of the diaphysis of a femur of the guinea-pig from which *A* and *B* were taken. The canals of blood vessels are dilated. Magnification, × 60.

THE APPEARANCE OF OSTEOID TISSUE IN THE BONES OF GUINEA-PIGS GIVEN INTERMITTENT TREATMENT WITH PARATHORMONE

The experiments thus far detailed showed that parathormone produces striking effects on the bones of young guinea-pigs. The changes in the bones observed forty-eight hours after one large dose were so severe as to result in cortical fractures in the regions where the cortex is normally thinnest—that is, at the costochondral junctions and at the metaphyses. Large doses induced, in addition, hemorrhage of the marrow, dilatation of the canals of blood vessels and slight fibrosis of the marrow. After repeated smaller doses, extensive fibrosis of the marrow and invasion of the enlarged canals of blood vessels by connective tissue occurred. After both single and repeated administration of parathormone, Howship's lacunae and osteoclasts were numerous.

In none of these experiments, in which the treatment was continuous, was there formation of osteoid tissue to any degree. In the experiments in which acute conditions were produced, no osteoid tissue appeared, for parathormone produced a constantly progressive resorption of bone, which would not permit the formation of osteoid tissue. In the experiments in which chronic changes resulted, the formation of osteoid tissue was not observed, except in the reparative process following fracture. It was because of this that we planned experiments in which we gave to some guinea-pigs intermittent treatment with parathormone, for we were desirous of observing the conditions under which extensive osteoid tissue appeared in guinea-pigs treated with parathormone.

Four guinea-pigs, each weighing between 235 and 410 Gm., were subjected to the daily injection of parathormone, beginning with a small dose, which was increased to 20 units by the fourth day. Treatment was continued with this dose until the seventh day. The treatment was then interrupted for seven days. On the fifteenth day it was resumed with the injection of 20 units daily until the twenty-first day in two animals and until the twenty-fourth day in the other two. The treatment was then again discontinued for five or six days. On resumption, the dosage was 20 units for one day, 30 units for one day, 40 units for two days and 60 units for one day. The treatment was discontinued, and the animals were killed after intervals of from three to seven days after the last injection.

One of the most striking features observed in connection with these animals was that the serum calcium of two of them was 8 and 7.4 mg. per hundred cubic centimeters. The guinea-pig which was allowed to live for seven days after the last injection of parathormone showed 10.2 mg. of serum calcium per hundred cubic centimeters. Two other guinea-pigs, not included in this series, which were also given inter-

mittent treatment, the dosages of which were stepped up to 50 units a day, and which were killed five days after the last injection of parathormone, showed 7.6 and 8.8 mg. of serum calcium per hundred cubic centimeters.

An examination of the bones of these animals suggested an explanation of the low serum calcium. Because of the large doses of para-

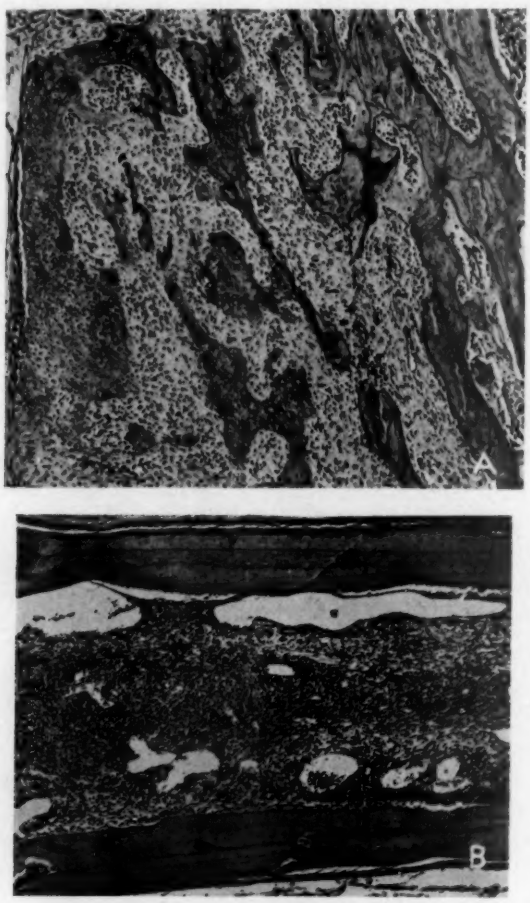


Fig. 6.—*A*, the shaft of a long tubular bone of a guinea-pig weighing 351 Gm. The animal was given intermittent treatment with parathormone and killed five days after the last injection. Note the extensive fibrosis of bone and the subperiosteal callus formation. Magnification, × 60. *B*, a rib of a guinea-pig given intermittent treatment with parathormone and killed four days after the last injection. There is hemorrhage of the marrow, with fibrosis and multiple cysts, some of which contain blood. Magnification, × 60.

thormone injected during the last few days of the treatment, extensive decalcification occurred, resulting in numerous fractures. A period of

active repair followed after the administration of parathormone had been discontinued, resulting in rapid and excessive deposition of calcium. This demand for calcium for purposes of bone repair may have been the cause of the lowered serum calcium.

During the period of repair the rate of formation of new bone, as demonstrated histologically, was rapid and the amount of new bone extensive. There was extensive subperiosteal callus formation, considerable new bone on the walls of the canals of blood vessels and considerable osteoid tissue at the costochondral junctions and in the metaphyses.

One of the animals showed numerous cysts in the marrow as a result of the extensive destruction of bone and marrow, and these cysts

Fig. 7.—The shaft of a long tubular bone, with considerable osteoid tissue repair, in the same animal from which *B* in figure 6 was taken. Magnification, × 130.

could frequently be identified as dilated vascular spaces secondary to the disturbance in the circulation in the marrow. Cysts and osteoid tissue (see figs. 6 and 7) were observed only in those animals that were allowed a few days to recover from the last dose of parathormone. It is therefore to be concluded that the formation of osteoid tissue and that of cysts, in the course of osteitis fibrosa, are features characteristic, not of the lesion produced by hyperparathyroidism, but of the repair of the lesion. The same conclusion regarding osteoid tissue in experimental and clinical hyperparathyroidism was reached by us as a result of our study of hyperparathyroidism in dogs.[1]

COMMENT

These experiments have shown that large doses of parathyroid extract (parathormone Collip) injected into young growing guinea-pigs cause severe lesions of the bones. The subcutaneous injection of one large dose of parathormone, 20 units per hundred grams of body weight, into young guinea-pigs produces destructive changes in their bones, and these lesions are characterized by resorption of bone (often very severe), fibrosis of bone, degeneration and fibrosis of marrow and cessation of the formation of bone at the zones of active growth. These lesions could not be definitely discerned before the twelfth hour, after which they progressed rapidly to the forty-eighth hour, and probably went on to repair after that. Extensive repair by subperiosteal formation of callus and production of osteoid tissue was found four days after the last injection of parathormone.

A striking observation in these young guinea-pigs given a large single dose of parathormone was that while ingestion of food was an important factor in moderating the effects of the injections of parathormone on the serum calcium and phosphorus,[3] the severe effects on the bones of young animals were present irrespective of fasting or feeding.

In contrast with the young, growing guinea-pigs, the fasting or fed adult guinea-pigs did not suffer appreciable histologic changes in the bones on injection of parathormone (20 units per hundred grams of body weight). However, there was a slight effect of the administration of parathormone on the serum calcium of these animals, more evident in the fasting adult animals. Whether the dosage for the adult animal was relatively too small, or whether the bone of the adult guinea-pig resists decalcification by parathormone in any dosage, we are not in a position to state at present. The problem of the effects of parathormone on adult guinea-pigs will be discussed in another paper.

After repeated injections of from 10 to 20 units of parathormone daily for about two weeks, histologic examination of the bones of young, growing guinea-pigs showed slight, but definite, resorption of bone and fibrosis of bone and marrow, although no clear effects had been observed on the serum calcium and phosphorus. After thirty-four days of treatment, a more definite effect on the bone and marrow was obtained, accompanied by a definite rise in the serum calcium and by normal phosphorus levels.

Animals receiving repeated large or moderate doses of parathormone all showed extensive lesions of the bones. Those receiving very large doses without having had preliminary treatment with parathormone showed destructive lesions in the bone and bone marrow. Extremely large doses of parathormone could be administered daily to guinea-pigs without the development of an overdosage complex, if

smaller or gradually increasing doses had been administered previously. Guinea-pigs were thus able to survive and maintain their weight for longer periods on large doses. Such animals showed resorption of bone and fibrosis of bone and marrow, but did not show the acute necrosis of marrow and the acute decalcification of bone that were observed in animals given one large dose or repeated large doses without preliminary treatment.

The question arises whether the lesions observed after daily injections of parathormone into guinea-pigs are to be designated as osteitis fibrosa. The changes observed in our experimental animals were as follows: generalized resorption of bone and enlargement of the canals of blood vessels; numerous Howship's lacunae and osteoclasts on the surfaces of the trabeculae, under the endosteum and periosteum, and on the walls of the canals of blood vessels; scarring of the bone marrow, and metastatic calcification in the gastric and intestinal mucosa, kidneys, heart, lungs and subcutaneous tissues. No osteoid tissue was observed. These changes are in every respect similar to those reported in the two cases of spontaneous fibrous osteodystrophy in rodents. When the question of the nature of the lesions in these animals was raised by the work of Lévy and Pick, the latter concluded, in agreement with others, that osteoid tissue was not necessary for making a diagnosis of osteitis fibrosa. Askanazy was the first to recognize "osteitis fibrosa without osteoid," in a case in man. In our experiments we have been able to show that osteoid tissue in fibrous lesions of the bones of guinea-pigs appears in the repair of the process initiated by hyperparathyroidism. We have found that if the destructive changes have been severe enough, the disturbances in the circulation in the marrow lead to the formation of cysts. We therefore believe that formation of osteoid tissue, hemorrhage of the marrow and formation of cysts occur only as secondary features and are not necessary for making the diagnosis of osteitis fibrosa in our experimental guinea-pigs. We further believe that these secondary features may also be produced experimentally with the same regularity as the primary features of osteitis fibrosa.

It remains to emphasize that the lesions produced in our experimental animals were a specific effect of experimental hyperparathyroidism. We have ruled out prolonged fasting as a factor in the experimental production of the acute changes. In the experiments in which chronic lesions resulted, the question of diet may be disposed of by the simple statement that the guinea-pigs were receiving their usual vegetable diet, which was proved adequate in mineral content and accessory food factors by our experience with untreated controls.

The lesions described were in every case generalized. While easier to study in the ribs, they affected all the bones examined. The changes

were most prominent at the costochondral junctions, in the metaphyses and in the diaphyses. The epiphyses did not show the specific effects of experimental hyperparathyroidism.

SUMMARY

The subcutaneous injection of one large single dose of parathormone into a young guinea-pig produces severe and rapid decalcification of the skeleton within forty-eight hours. Age also seems to be a factor in the production of lesions of the bones after single injections of parathormone. Adult guinea-pigs given injections (20 units per hundred grams of body weight) did not show changes in the bones forty-eight hours after the injection. After repeated daily injections of smaller doses of parathormone, resorption of bone and fibrosis of bone and marrow result. The lesions observed after daily injections of parathormone into guinea-pigs are of the same order as those described for osteitis fibrosa without osteoid tissue in man. Osteoid tissue and cysts in the marrow may appear during the repair of severe lesions in experimental hyperparathyroidism of guinea-pigs.

INVASION OF THE FALLOPIAN TUBE BY OXYURIS VERMICULARIS

REPORT OF A CASE *

W. J. JONES, M.D.
LA CROSSE, WIS.
AND
C. H. BUNTING, M.D.
MADISON, WIS.

The case here published is presented as adding to the data accumulating which seem to show that the widespread parasite *Oxyuris vermicularis* (or more properly *Enterobius vermicularis*) is not to be dismissed too lightly as of little clinical or pathologic importance.

REPORT OF CASE

History.—One of us (W. J. J.) was called to see, in his practice, Miss M. V., a white woman, aged 22, who complained of a pain in the lower right side of the abdomen, which had begun two days previously, and which was becoming more severe. It was associated with nausea and vomiting.

Several points in the patient's history proved of interest and importance. She stated that for ten years she had been subject to intense perineal and anal itching, worse at night, and that her mother and one brother were similarly affected. About four months previously, the patient had a severe pain low down in the left side of the abdomen, which was worse on walking or on jarring. As this was coincident with the onset of menstruation (which on this occasion was manifested by an excessive flow lasting eight days as against a usual four or five day flow), the pain was attributed to this factor. She said that she had not had venereal infection.

Examination.—On examination, the patient was found to have marked tenderness in the lower right abdominal quadrant, with distinct rigidity of the muscles of the right side. There was some tenderness in the lower left quadrant. No masses were palpated. Except for slight diffuse bilateral enlargement of the thyroid gland, the general examination revealed no gross abnormality.

The pulse rate was 95; red blood cells, 4,600,000; hemoglobin, 75 per cent; leukocytes, 11,700; temperature, 99.8 F.

Diagnosis and Operation.—A diagnosis of acute appendicitis was made, and appendectomy was performed.

At operation, through a right rectus incision, the acutely inflamed appendix was found coiled on itself in the pelvis, to the wall of which it was bound by light, easily broken adhesions which did not interfere with its satisfactory removal. A large cyst of the right ovary was treated by puncture and removal, the remaining ovarian tissue being left in situ.

The left ovary and fallopian tube were bound down in the pelvis by dense adhesions and were delivered with difficulty. The tube showed a distinct inflam-

* Submitted for publication, Aug. 8, 1930.

matory condition, and its distal half was distended into an abscess about 1 inch (2.5 cm.) in diameter. The ovary was enlarged and dense, and apparently contained areas of calcification. Ovary and tube were removed, and the abdominal wound was closed.

Course.—Convalescence was without interruption, and the patient was discharged on the fourteenth day.

Four weeks later the patient returned with the complaint of intense midline pain low down in the abdomen. The patient was examined under anesthesia, and

Fig. 1.—Low power view of the wall of the fallopian tube with invading parasite.

there was found an intense inflammation of the vagina with the cervix swollen and eroded in several areas and exuding a slimy discharge. Dilatation and curettage were done.

In the year following this operation, the patient was well and had no recurrence of pelvic symptoms.

Gross Pathologic Examination.—The appendix showed a definite acute inflammatory reaction. When opened, it was found to contain several fecal concretions and twenty or more small worms from one-fourth to one-half inch (0.61 to

Fig. 2.—High power view of a part of the parasite and of the necrotic field surrounding it.

1.27 cm.) in length. These were alive and active, even after the appendix had been out of the body for some time.

The left fallopian tube showed a marked purulent salpingitis, which converted its distal half into a pus-containing cavity about 1 inch (2.5 cm.) in diameter. The wall of the tube was definitely thickened in this area. No worms were found in the exudate.

A part of the thickened wall of the tube was sent to the Pathological Laboratory of the University of Wisconsin for histologic examination.

Histologic Examination of Fallopian Tube.—The tubal tissue received in formaldehyde was mounted in paraffin and sectioned perpendicular to the peritoneal surface. As the first section cut showed an area of necrosis suggestive of tuberculous caseation, but without the histology of a tuberculous lesion, a short series of sections was cut in an effort to find the etiologic agent. The finding of the ova of *Oxyuris vermicularis* led to further serial sections, until there was disclosed a female oxyurid lying in the wall of the tube and curled on itself, as shown in the low power photograph (fig. 1). The cuticle of the worm was well preserved, but not intact, and the parasite was heavily loaded with ova, as shown in the photograph at higher power (fig. 2). That the defects in the cuticle were not artefacts was shown by the fact that in certain areas there was a marked invasion of the worm by leukocytes, a considerable proportion of which were eosinophils. The parasite was surrounded throughout by a zone of necrosis. The necrotic cells were chiefly leukocytes, although in certain areas there was definite necrosis of tubal tissue. Among the dead leukocytes, there was evidence of a marked eosinophil participation in the exudation. In fact, the living polymorphonuclear leukocytes at the tissue edge of the necrotic zone were almost entirely eosinophil. Mononuclear phagocytes were conspicuously absent. About the zone of necrosis there was well marked connective tissue encapsulation, with a moderate infiltration by lymphocytes, plasma cells and eosinophil leukocytes. The epithelial and peritoneal surfaces of the tubal section were intact. There was an inflammatory dilatation of the vessels beneath the epithelium and some leukocytic and lymphocytic exudation.

The impression was gained that the parasite had burrowed into the tubal tissue along the sulci between the major folds and not directly into the wall at the point where it was found, as no sign of injury was seen in the tissue or in the epithelium immediately over the worm. As shown in figure 1, the oxyurid lay almost equidistant from the epithelium and the peritoneal covering of the tube.

Histologic sections of the ovary showed an atrophic, sclerotic organ with old fibrous adhesions attached to the surface. There was no evidence of further parasitic involvement.

Curettings from the uterus showed a chronic endometritis with definite, extensive fibroblastic proliferation. No lesion was found other than hemorrhage, which was apparently due to the curretting.

SUMMARY

In a woman 22 years old, with a history of prolonged perineal nocturnal itching and with symptoms of pain and tenderness in the lower part of the abdomen, accompanied by fever and leukocytosis, there was found at operation: (1) acute appendicitis, with many nematodes of the genus *Oxyuris vermicularis* in the lumen, and fecal concretions, and (2) acute salpingitis, with a female oxyurid embedded

in the wall of the tube. Unfortunately, cultures were not made from the appendix or from the tube, and the appendix was not saved for section.

According to Heller,[1] the embryo oxyurids emerge from ova high up in the intestine, develop gradually in their slow progress down the intestine, until, in about two weeks, they reach the cecum in a sexually mature stage. Here and in the appendix conjugation takes place, and the worms remain in these parts longer than in any other part of the intestine. The mature females eventually move gradually down the colon, laying their eggs on fecal masses and on the skin when they wander out of the anus at night. Heller regards the presence of *Oxyuris* in the lumen of the appendix as of no pathologic significance. This would seem to be true. However, as is shown definitely in the reports of Cecil and Buckley [2] and of Rheindorf, the worm may invade the wall of the appendix and may possibly penetrate even to the serosa. This raises the question of the part played by the worm in initiating appendicitis. Cecil and Buckley concluded from their study that there is a definite and characteristic form of appendicitis produced by *Oxyuris* and *Trichocephalus*. Rheindorf [3] was of the same opinion. Aschoff,[4] in controversy with Rheindorf, took an opposite position and spoke of a "pseudo-appendicitis."

The present case can add no evidence on either side of the controversy, as the appendix was not studied histologically to determine whether or not it was invaded. It would seem from the cases of Weigmann [5] and Vuillemin [6] that the worm may penetrate the intestinal wall and either of itself or through bacteria carried with it initiate suppurative processes. Weigmann, in a boy of 6, found on each side of the anal opening a perirectal abscess containing living oxyurids and scattered ova; and Vuillemin quoted his confrere Froelich as having found in a boy of 11, a perirectal abscess containing sixty female oxyurids. In neither case was gross communication found between the abscess and the intestinal lumen.

Nathan (quoted by Chiari [7]) reported a somewhat similar case of a young laborer with a perirectal abscess that would not "ripen" under ordinary treatment. The abscess showed eggs of *Oxyuris*, but no bacteria, when examined pathologically after operation.

---

1. Heller: Deutsches Arch. f. klin. Med. **77**:21, 1903.
2. Cecil and Buckley: Am. J. M. Sc. **143**:793, 1912.
3. Rheindorf: Zentralbl. f. Bakteriol. **74**:604, 1914.
4. Aschoff: Berl. klin. Wchnschr. **57**:1041, 1920.
5. Weigmann: Berl. klin. Wchnschr. **58**:732, 1921.
6. Vuillemin: Zentralbl. f. Bakteriol. **32**:358, 1902.
7. Chiari: Virchows Arch. f. path. Anat. **269**:730, 1928.

A similar question arises in regard to the relationship of *Oxyuris* to lesions in the female generative tract. One must assume that the female parasite in its out-wanderings at night gets into the vagina much oftener than references in the literature would suggest. It must commonly therefore not produce lesions there.

That the worm may traverse the whole genital tract and become implanted and encapsulated on the peritoneum without symptoms is definitely indicated by the finding of such nodules accidentally at operation or at postmortem examination. Goodale and Krischner [8] recently reported such a case and collected from the literature six others, all in women. Their case was in a woman of 21, in whom, in the course of an operation, several loops of the pelvic small bowel were found covered with hard, white nodules, each slightly smaller than a pea. These nodules were diagnosed as tubercles, but when one was sectioned it was found to contain a female oxyurid filled with ova.

Marro [9] reported the occurrence in a woman of 34 of a cyst implanted on the fallopian tube near the fimbriated extremity. This had a wall 2 mm. thick and contained the ova of *Oxyuris*, granular detritus and cholesterol crystals.

In a 42 year old woman who had died of cancer of the breast, Kolb [10] found ten nodules of the size of a grain of rice scattered in the pelvic peritoneum. One of these on section showed a female oxyurid surrounded by granular detritus, giant cells and a connective tissue capsule.

Schneider [11] found in the culdesac of a 36 year old patient who had died of peritonitis after a hysterectomy an encapsulated cyst 2 cm. in diameter, which contained a female worm.

Strada [12] found an encapsulated oxyurid in the culdesac of a woman of 60 who had died of bronchopneumonia.

Schroeder [13] is quoted by Chiari as having seen a similar case.

Kaufmann's [14] case of ova of *Oxyuris* in one of numerous caseous nodules seen on the colon and mesocolon of a woman of 31, at an abdominal operation, is perhaps not so clearly an infestation of the peritoneum by the genital route.

In all of these cases there was set up a sharply localized inflammatory reaction, resulting eventually in encapsulation, and in no case was there

8. Goodale and Krischner: Arch. Path. **9**:631, 1930.
9. Marro: Gior. d. r. Accad. di med. di Torino **7**:251, 1901.
10. Kolb: Zentralbl. f. Bakteriol. **31**:268, 1902.
11. Schneider: Zentralbl. f. Bakteriol. **36**:550, 1904.
12. Strada, quoted by Goodale and Krischner (footnote 8).
13. Tschamer: Zentralbl. f. Gynäk. **43**:989, 1919.
14. Kaufmann: Pathology for Students and Practitioners (Reimann's translation of Lehrbuch der pathologischen Anatomie), Philadelphia, P. Blakiston's Son & Company, 1929, vol. 2, p. 855.

a general peritoneal reaction. In none of these cases was there note of pathologic effects in the uterus or in the tube.

Tschamer's [15] finding of two living worms in the fallopian tube at total hysterectomy for chorionic epithelioma in a patient of 31, without evidence even histologically of local reaction, confirms the possibility of a passage of the worm without the production of lesions.

We have been able to find in the literature only two references to invasion of the wall of the tube by *Oxyuris:* the case of Strasser and that of Chiari.

Strasser's [16] case was that of a woman of 26 with tuberculous peritonitis, in the wall of whose fallopian tube there were found calcified masses, singly, in clumps and in long packets. These were surrounded by foreign body giant cells, and there was a marked fibrous alteration of the wall of the tube adjacent to them. When decalcified, these masses were found to be ova of *Oxyuris.* The reaction here was evidently similar to that in the peritoneum.

Chiari's [7] case corresponds closely with that reported here. A young woman of 20 who had had symptoms of pelvic inflammation six months previously was seized suddenly with sharp pain low in the abdomen and had fever and vomiting, but no vaginal discharge. Tenderness in the right side on pressure led to a diagnosis of right salpingitis, and to operative removal of that tube. Examination of the tube showed a swelling to 4.5 cm. of the distal portion, with a hard, scarlike thickening of the wall, a milky, purulent, blood-tinged content and light peritoneal adhesions. In section, there was encountered a female oxyurid partly in a crypt and partly embedded in the mucosa of the tube—with a definite zone of necrosis about it, and with a sharp eosinophil reaction, corresponding clearly to the reaction in this case. No cultures were made, but no bacteria were found in smears of the tubal exudate or in section. Chiari expressed the opinion that the worm was responsible for the salpingitis.

It would seem that we might conclude from our case and those reported in the literature, that *Oxyuris vermicularis* may be present in the lumen of the appendix or in that of the genital tract in women without producing definite lesions or symptoms, but that on invasion of the wall of any viscus it may be responsible for a definite inflammatory reaction, in which exudation of eosinophil leukocytes is a prominent feature. Ordinarily, encapsulation ensues. Occasionally, a suppurative process results. Whether the latter lesion is due entirely to *Oxyuris* or in part to associated bacteria is not definitely determined by the cases thus far reported.

15. Tschamer: Zentralbl. f. Gynäk. **43**:989, 1919.

16. Strasser: Inaugural Dissertation, Bonn, 1915.

MAMMARY GLAND SITUATED ON THE LABIUM MAJUS

REPORT OF A CASE *

JOSEPH McFARLAND, M.D.
PHILADELPHIA

In March, 1930, A. R., a colored woman, aged 34, married, who had progressed about six months in her third pregnancy, was admitted to the psychopathic ward of the Philadelphia General Hospital, in the service of Dr. Max H. Bochroch. She was not long in the ward before it was discovered that she had a rounded, pendulous body attached by a broad and not long pedicle to the lower third of the right labium majus. The general surface of the skin covering it was smooth and without hairs. Pressure showed the body to be slightly sensitive. The patient was carefully questioned as to the duration of the lesion, but her mental state was such that none of her statements could be considered as without great probability of error. She, however, asserted that it had made its appearance shortly after the beginning of the present pregnancy, never having been recognized before.

After careful examination and consideration, the diagnosis of fibroma of the vulva was reached. The intern, Dr. Joseph Parrish, was authorized to remove it, which he did on March 19, 1930.

The tissue received at the laboratory measured 5 by 3 by 2.5 cm. It was covered with deeply pigmented skin (the patient was a rather dark Negress) that had retracted into folds. Beneath the skin was an encapsulated node, so loosely attached that it seemed to be separating itself from its surroundings. It seemed to consist of several lobulations.

When cut through, the structure was the same throughout and appeared coarsely granular and porous, so that the diagnosis was changed from fibroma to adenoma. There was a peculiar pale yellowish color that seemed to be the result of the glandular substance, which was yellowish, alternating with pinkish-white stroma.

Microscopic sections were prepared and were expected to show adenoma of Bartholin's gland, but instead showed typical mammary tissue of advanced pregnancy. The yellowish tinge was found to

* Submitted for publication, June 30, 1930.

* From the McManes Laboratory of Pathology of the University of Pennsylvania and the Pathological Laboratory of the Philadelphia General Hospital.

be caused by the considerable quantity of fat in the vacuolated secretory cells.

The gross appearance of the interesting abnormality is shown in the accompanying drawing, a sketch made by Dr. Parrish, who performed the operation. Photomicrographs of the sections under low and high power lenses are also shown. Photomicrographs, under the same magnifications, of sections from the normal pectoral mamma of a woman

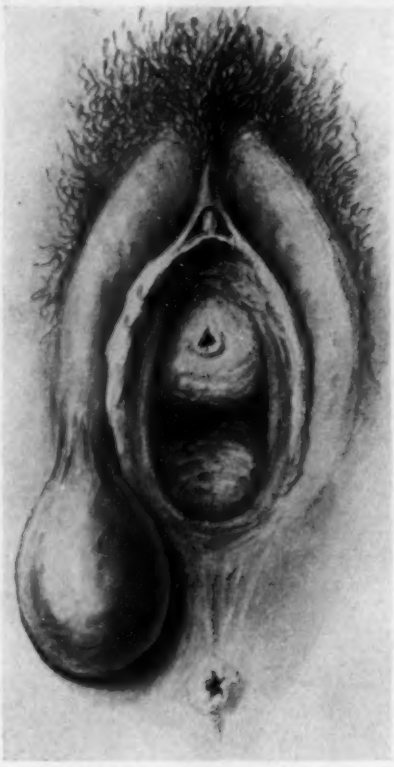


Fig. 1.—Drawing of mammary gland situated on the labium majus, at the sixth month of pregnancy.

at the same stage of pregnancy were compared, and the resemblance of these to the two was such that in arranging the latter for publication it was necessary to refer to the numbers published on the photographs in order not to confuse them.

I communicated my interest in this rare malformation to Dr. Bochroch, who gave me the specimen, together with the necessary data and permission to publish a report of the case. Dr. Parrish supplied the sketch.

As is well known, the milk lines run diagonally from the axillary to the pubic regions, many mammary rudiments appearing in the embryos of all mammals, to be developed or suppressed according to the phylogenesis of the particular group under consideration. In man, all are normally extinguished, except one on each side in the pectoral region; in the cetacea, all disappear, except one on each labium majus vulvae. When suppression of any of the rudiments fails, supernumerary mammae develop. In this case one of the rudiments so placed as later to be

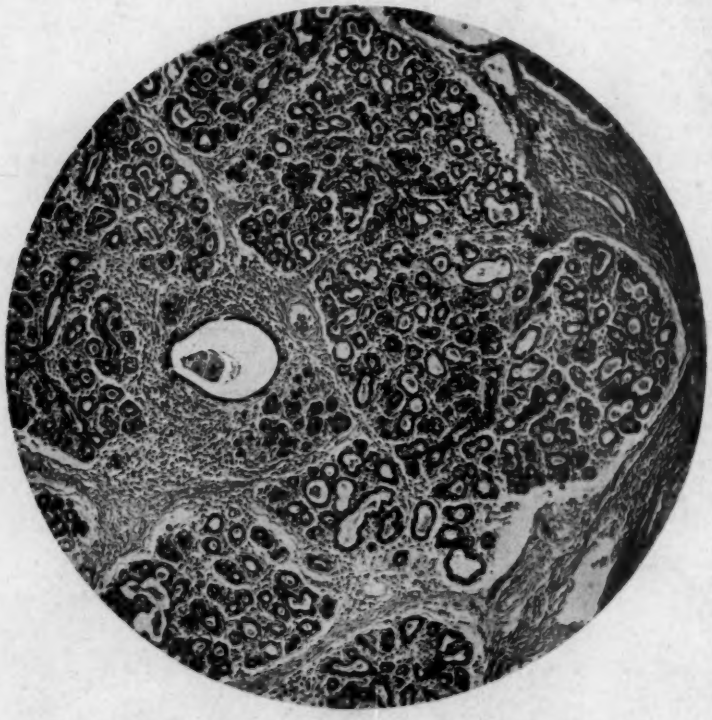


Fig. 2.—Section of the vulvar mamma described in this report.

situated on a labium majus survived, with the occurrence of a mammary gland in a rare situation.

The case is, however, not unique. Hartung [1] described what appears to be the first case published. The subject was a woman, aged 30, to the lower inner aspect of whose left labium majus a body the size of a goose egg was attached by a pedicle the size of a man's thumb. It was congenital. It had enlarged at puberty, was wont to manifest changes coinciding with the menstrual periods and exuded a milky fluid from an eroded area on the upper anterior surface, where careful examination

1. Hartung: Inaugural Dissertation, Erlangen, 1872.

revealed a retracted nipple surrounded by a shallow depression. It was removed and, when examined microscopically, proved to be a fully developed mammary gland.

De Blasio [2] observed a young woman who had a mammary gland the size of a hen's egg on the outer side of each labium majus, surmounted

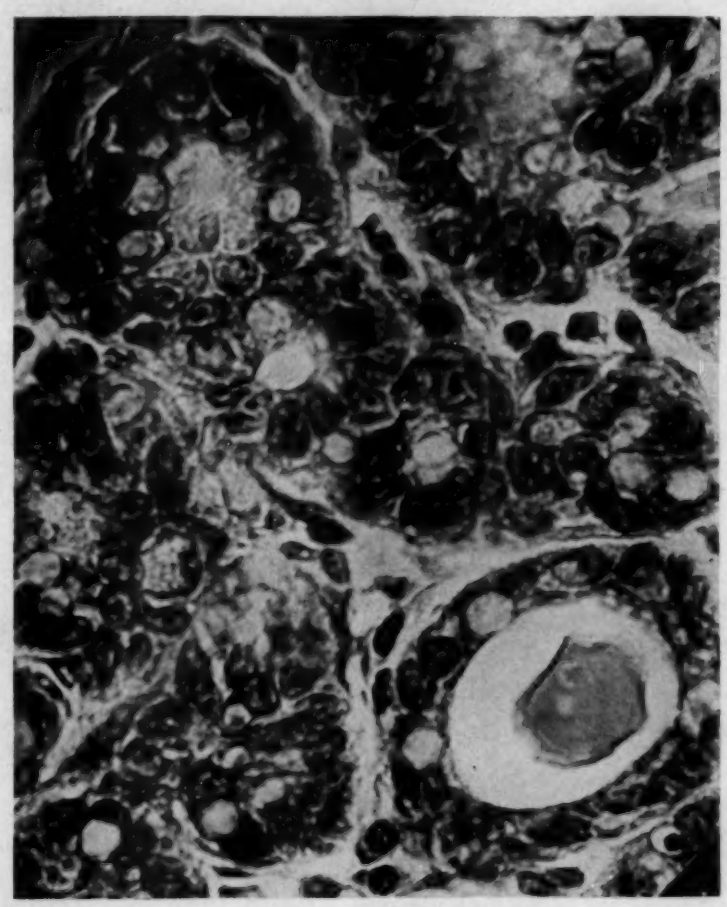


Fig. 3.—Section of the vulvar mamma magnified to show the fat vacuoles in the cells and jelly-like cylinders caused by the coagulation of proteins in the colostrum being condensed by the fixative—a picture identical with that of a similarly magnified section of normal pectoral mamma of a woman about eight months pregnant.

by a well formed nipple. To the age of puberty only the nipples were visible, the glands developing later. It was during pregnancy that the maximum size and development were reached.

2. de Blasio: Arch. di psichiat., Torino **24**: 171, 1905.

Bell [3] reported the case of a multipara, aged 59, who had a body the size of a hen's egg attached just in front of the left labium majus by a pedicle 3 cm. in diameter. It was of variable consistency, elastic and unattached to the skin that slid over it easily. When removed and examined microscopically, it showed a structure identical with the resting mammary gland.

The case herein reported seems, therefore, to be the fourth noted occurrence of this rare anomaly.

It is unfortunate that the patient suffered from mental disturbance, as it prevented us from learning how the gland behaved in her earlier pregnancies. Theoretically, it should have evolved and retrogressed with each.

---

3. Bell: Am. J. Obst. & Gynec. **11**:507, 1926.

THE RESPONSE OF BLOOD PLATELETS TO EXTERNAL STIMULI: ULTRAVIOLET LIGHT, IODINE AND COAL TAR*

PAUL E. STEINER, M.S.
AND
FRANCIS D. GUNN, M.D.
CHICAGO

The number of blood platelets in healthy animals is fairly constant, though daily and even hourly fluctuations of considerable volume occur. In general, the level is not as constant as that of erythrocytes, but is more constant than that of leukocytes. Spontaneous variations, when they occur, can usually be explained on the basis of infections or of alterations of the environment, especially changes in light. In experimental procedures devised to study the problems of the origin and the function of the blood platelets, a great variety of agents have been employed for altering the platelet content of the blood. Recently, some of these methods have been used clinically in man in attempts to influence the course of disease in which the number of platelets has been pathologically altered.

The effective agents can be divided roughly into internal and external. The former, including toxic and irritating substances, especially bacterial toxins introduced into the blood stream, intravenous injections of particulate matter, infections, splenectomy and hemorrhage, have been studied extensively by numerous workers. The latter, consisting chiefly of the different forms of radiant energy, have received but little attention until recent years.

In 1913, Duke [1] studied the effects of benzene and diphtheria toxin and found that with fatal doses the number of circulating platelets was decreased while with nonfatal doses their number was increased. Large doses of tuberculin were necessary to produce a similar response. Weiskotten, Wyatt and Gibbs [2] and Hultgren [3] corroborated his results

* Submitted for publication, Aug. 12, 1930.

* From the Department of Pathology, Northwestern University Medical School.

1. Duke, W. W.: Causes of Variation in the Platelet Count, Arch. Int. Med. **11**:100, 1913.

2. Weiskotten, H. G.; Wyatt, T. C., and Gibbs, F. R. D.: The Action of Benzol: VII. Thrombocytopenia and Thrombocytosis Coincident with Marrow Necrosis and Marrow Regeneration (Rabbit), J. M. Research **44**:593, 1924.

3. Hultgren, G.: Action du benzol sur la teneur du sang en thrombocytes, leucocytes et érythrocytes, Compt. rend. Soc. de biol. **95**:1060, 1926.

with benzene. Many earlier authors, and more recently Bannerman,[4] found an increased platelet count in pulmonary tuberculosis, the higher levels occurring most commonly in the progressive cases.

In 1915 Duke [5] stated that the platelets are usually decreased in number during the febrile stage of acute infectious diseases and increased in number during convalescence. Reimann,[6] in studies of the behavior of blood platelets during the course of pneumonia in man, and in experimentally infected rabbits, found that thrombopenia occurs during the febrile period, and that the normal number is greatly exceeded during the postfebrile period following the crisis.

Particulate matter introduced into the blood stream sometimes produces a rise and sometimes a fall in the number of platelets. Suspensions of killed bacteria (Duke [5]) and carbon particles (Bedson [7]) have been found to produce considerable increases. Beronius,[8] Koster [9] and Cramer and Bannerman [10] reported increases in platelets following the injection of trypan blue. Injections of colloidal lead (Brookfield [11]), india ink (Bedson [7]) and many other agents of a particulate nature have been reported as effective in increasing the number of blood platelets.

That sudden, severe hemorrhage is followed by a rapid regeneration of platelets was demonstrated in 1911 by Duke [12] and corroborated later by Petri.[13]

---

4. Bannerman, R. G.: Blood Plate Counts in Pulmonary Tuberculosis, Lancet **2**:593, 1924.

5. Duke, W. W.: Variation in the Platelet Count; Its Cause and Clinical Significance, J. A. M. A. **65**:1600, 1915.

6. Reimann, H. A.: A Study of the Behavior of Blood Platelets in Pneumococcus Infections, J. Exper. Med. **40**:553, 1924.

7. Bedson, S. P.: The Rôle of the Reticulo-Endothelial System in the Regulation of the Number of Platelets in the Circulation, Brit. J. Exper. Path. **7**:317, 1926.

8. Beronius, H.: Action du bleu trypan sur la formule sanguine du lapin, Compt. rend. Soc. de biol. **99**:1675, 1928.

9. Koster, H.: Reticulo-Endothelial System. Platelets, J. Exper. Med. **44**:75, 1926.

10. Cramer, W., and Bannerman, R. G.: Clinical Significance of Blood Platelets, Lancet **1**:992, 1929.

11. Brookfield, R. W.: Blood Changes Occurring During the Course of Treatment of Malignant Disease by Lead, with Special Reference to Punctate Basophilia and the Platelets, J. Path. & Bact. **31**:277, 1928.

12. Duke, W. W.: The Rate of Regeneration of Blood Platelets, J. Exper. Med. **14**:265, 1911.

13. Petri, S.: III. Experiments by a Special Bleeding Technique to Produce Isolated Influencing of Blood Platelets and Their Source, Acta path. et microbiol. Scandinav. **2**:23 and 277, 1925.

Myers and his associates,[14] Evans,[15] Washburn [16] and many others have reported increased numbers of blood platelets after splenectomy. Bachman and Hultgren [17] also found an increase after splenectomy, but obtained similar results by traumatizing the mesentery and putting sutures into it. Liles [18] observed a rise after operative procedures. Dawbarn and his associates [19] counted platelets in a large series of cases in the hospital and found their numbers increased after operations of all kinds, childbirth and fractures. They suggest that the common factor is injury to tissue with absorption of the products of protein disintegration.

Binet and Kaplan [20] observed that after asphyxia in dogs the platelet level was elevated for about an hour. This did not occur if splenectomy had been previously performed. Epinephrine (Binet and Kaplan [21]), given to cause contraction of the spleen, produced a similar rise. The rise did not occur after splenectomy or after the administration of yohimbine to prevent contraction of the spleen.

The external agents studied have consisted chiefly of different forms of radiant energy—sunlight, x-rays and radium emanations.

Cramer, Drew and Mottram [22] found that large doses of radium produced a decided fall in the number of platelets. Fabricius-Möller [23]

---

14. Myers, B.; Maingot, R., and Gordon, A. K.: Three Cases of Splenectomy for Essential Thrombocytopenic Purpura Hemorrhagica, Proc. Roy. Soc. Med. (Clin. Sect.) **19**:37, 1926.

15. Evans, W. H.: The Blood Changes after Splenectomy in Splenic Anemia, Purpura Hemorrhagica and Acholuric Jaundice, with Special Reference to Platelets and Coagulation, J. Path. & Bact. **31**:815, 1928.

16. Washburn, A. H.: Splenectomy in Thrombocytopenic Purpura, J. A. M. A. **94**:313, 1930.

17. Bachman, E. L., and Hultgren, G.: Influence de l'intervention chirurgicale en particulier de l'extirpation de la rate sur la teneur du sang en thrombocytes, Compt. rend. Soc. de biol. **94**:942, 1926.

18. Liles, R. T.: Blood Platelets in Rabbits Following Splenectomy and Transplantation of the Spleen, Proc. Soc. Exper. Biol. & Med. **23**:489, 1926.

19. Dawbarn, R. V.; Erlam, F., and Evans, W. H.: The Relation of the Blood Platelets to Thrombosis after Operation and Parturition, J. Path. & Bact. **31**:833, 1928.

20. Binet, L., and Kaplan, M.: Mobilisation des plaquettes par l'asphyxie. Origine splénique de la plaquettose asphyxique, Compt. rend. Soc. de biol. **97**:1128, 1927.

21. Binet, L., and Kaplan, M.: Mobilisation des plaquettes par l'adrénaline. Plaquettose par spléno-contraction adrénalinique, Compt. rend. Soc. de biol. **97**: 1659, 1928.

22. Cramer, W.; Drew, A. H., and Mottram, J. C.: Similarity of Effects Produced by Absence of Vitamines and by Exposure to X-Rays and Radium, Lancet **1**:963, 1921.

23. Fabricius-Möller, A.: Études expérimentales sur la diathèse hémorrhagique detérminée par les rayons Roentgen, Compt. rend. Soc. de biol. **87**:759, 1922.

reported thrombopenia from massive doses of x-rays. Mottram [24] observed transitory thrombocytosis after smaller doses of radium. Cramer and Drew [25] showed that rats kept in darkness from birth had a lower platelet count than those reared under normal light conditions, and in these rats, exposure to the mercury vapor quartz lamp for short daily periods caused the platelet level to rise rapidly toward normal. Laurens and Sooy [26] found that growing albino rats had a lower platelet count at the end of six months if kept in darkness than if exposed to diffuse daylight or to direct sunlight. Sooy and Moise [27] treated ten patients suffering from purpura with the mercury vapor quartz lamp, and observed increases in the number of blood platelets and abatement of symptoms. In one case, the platelet count increased from 108,000 to 546,000. Gunn,[28] working with young rabbits, exposed the shaved back daily to the mercury vapor quartz lamp and found a temporary increase in the platelet count. Miles and Laurens [29] showed that in dogs kept in darkness the number of platelets was lowered and that there was a rise above normal followed by a gradual return to normal when the animals were returned to light. They then tried the effect of carbon arc radiation and obtained an increase in the platelets after temporary depressions. Hardy [30] repeated and extended the experiments of Gunn on rabbits, carefully measuring the intensity and the wave length of the light used. Sanford [31] studied the effect of ultraviolet light on infants 4 days old, and found that the number of platelets was temporarily increased. Mayerson and Laurens [32] found a slight rise

---

24. Mottram, J. C.: Some Effects of Exposure to Radium on the Blood Platelets, Proc. Roy. Soc. Med. (Sect. Path.) **16**:9, 1923.

25. Cramer, W., and Drew, A. H.: The Effect of Light on the Organism, Brit. J. Exper. Path. **4**:271, 1923.

26. Laurens, H., and Sooy, J. W.: The Effect of Light and of Darkness on the Blood Cell Count of the Growing Albino Rat, Proc. Soc. Exper. Biol. & Med. **22**:114, 1924.

27. Sooy, J. W., and Moise, T. S.: Treatment of Idiopathic Purpura Hemorrhagica, J. A. M. A. **87**:94, 1926.

28. Gunn, F. D.: The Influence of Ultraviolet Light upon Blood Platelets in Young Rabbits, Proc. Soc. Exper. Biol. & Med. **24**:120, 1926.

29. Miles, A. L., and Laurens, H.: III. The Effects of Darkness on Some of the Physical Characters of the Blood of Dogs, Am. J. Physiol. **75**:443, 1926; IV. The Effects of Carbon Arc Radiation on Some of the Physical Characters of the Blood of Dogs, Am. J. Physiol. **75**:462, 1926.

30. Hardy, M.: The Effect of Measured Amounts of Ultraviolet Radiation on the Blood Count of Normal Rabbits, Am. J. Hyg. **7**:811, 1927.

31. Sanford, H. N.: Effect of Ultraviolet Light on the Blood of New-Born Infants, Am. J. Dis. Child. **33**:50, 1927.

32. Mayerson, H. S., and Laurens, H.: The Effect of Carbon Arc Radiation on the Blood of Dogs, Am. J. Physiol. **86**:1, 1928.

following exposure to the carbon arc in dogs, which persisted for about ten days. Vannfalt [33] corroborated the work of Gunn on rabbits, and also observed an increase in the human being treated with ultraviolet rays.[34] This increase varied greatly with dosage and individual susceptibility.

The mechanism by which the radiation causes a rise in blood platelets is not understood. The evidence furnished by experiments with darkness and sunlight and the results reported recently by Phillips and Robertson [35] with feeding of viosterol indicate a photochemical effect in the skin, possibly by the action of light on lipoids in the skin. On the other hand, the almost constant occurrence of thrombocytosis after operative procedures involving trauma to tissues would suggest that the effect might be brought about by the absorption of products of the destruction of tissue at the site of injury (i. e., in the skin), and that these products may be the effective stimuli for the production of platelets.

The experiments reported in this paper were suggested by an observation made during the course of an experiment with ultraviolet light. It was noticed that the platelet count was sometimes increased after the animal's back was shaved preliminary to treatment with the ultraviolet lamp, particularly if the skin was lacerated. This suggested that it might be advantageous to investigate the effects on the blood platelet level, of various irritants applied locally to the skin. By this means it was hoped that some information might be obtained with regard to the specificity of the effects of ultraviolet light and possibly with regard to the nature of the stimulus or stimuli competent to affect generation of platelets. This paper will describe alterations in the blood picture coincident with inflammatory reactions in the skin of young rabbits, produced by ultraviolet light and by local applications of iodine and of coal tar.

NORMAL BLOOD COUNTS OF RABBITS

Before experimental alteration of the number of the blood platelets was attempted, the formed blood elements were counted daily for several days in order to establish the normal level for each animal.

Method.—Fourteen miscellaneous stock rabbits, varying in weight from 980 to 2,915 Gm., were usedf or the experiments. Blood counts were made daily at approximately the same hour. The method used for counting platelets was an

33. Vannfalt, K. A.: Action des rayons ultraviolets sur la teneur du sang du lapin en leucocytes et en thrombocytes, Compt. rend. Soc. de biol. **101**:607, 1929.

34. Vannfalt, K. A.: Action de la lumière ultraviolette sur la composition du sang humain, Compt. rend. Soc. de biol. **101**:610, 1929.

35. Phillips, R. A., and Robertson, F. D.: Effect of Irradiated Ergosterol on Mammalian Thrombocyte Counts, Proc. Soc. Exper. Biol. & Med. **26**:639, 1929.

indirect one in which stained films were used (Gunn and Vaughan[36]). The blood films were stained with Wright's blood stain, covered with oil and coverslip and counted under the high power, dry lens. A minimum of 1,000 erythrocytes was counted, with the platelets in the corresponding fields. From this ratio of platelets to erythrocytes the total number of platelets per cubic millimeter was calculated. Leukocyte and erythrocyte counts were made at the same time by the usual methods. Whenever there was a marked change in any of the elements, that count was repeated at once with a new blood specimen.

The animals were fed on the standard laboratory diet of carrots, oats and water daily, and alfalfa two or three times a week. The pens were kept in room light, but out of direct sunlight. The rectal temperature was taken daily and the weight frequently.

Results.—For periods of from four to eleven days preceding the experiment proper, the average for the group of fourteen rabbits was 980,000 platelets per cubic millimeter. There was considerable difference in the different animals; the lowest average was 626,000 and the highest, 1,619,000. In one case the daily variation was as much as 60 per cent. The animals exhibiting the highest platelet levels showed the greatest daily variation in counts.

The leukocyte average for this group was 11,051 per cubic millimeter. Here, also, there was considerable daily variation. The averages for the control period were between 6,450 and 14,867. Occasional high counts were found for one day, but were unaccompanied by any rise in temperature. Bachman and his associates[37] found that when the platelet level was high, the leukocyte count also was high. We were unable to find any such correlation in our counts.

The erythrocyte average was 5,961,780 for the series. The variation in different animals was between 5,120,000 and 6,836,000. The level in individual animals is rather constant. However, if water is withheld or for any reason the rabbits refuse to take food and liquids, they may become quickly dehydrated, with a correspondingly rapid rise in the erythrocyte count.

Comment.—These results emphasize the necessity for studying carefully the platelets of any given rabbit for an adequate period of time prior to any experimental procedure, in order to establish the normal variation for this animal. Even then the results must be interpreted with caution. Considerable variation is to be expected in the rabbit. Binet and Kaplan[21] showed that after injections of epinephrine to cause contraction of the spleen, there may be a 100 per cent increase in the number of circulating platelets, persisting for about one hour. It is

36. Gunn, F. D., and Vaughan, S. L.: Bone Marrow Reactions: II. The Blood Count in the Albino Rat: Blood Platelets, Anat. Rec. **45**:59, 1930.

37. Bachman, E. L.; Edström, G.; Grahs, E.; Hultgren, G., and Price, H.: Teneur du sang du lapin en plaquettes et en globules blancs, Compt. rend. Soc. de biol. **91**:1089, 1924.

known that the spleen contracts in times of emotional excitement, so that fright in the animal during the collection of the blood specimens might cause considerable variation in susceptible animals.

Comparison of the platelet counts in rabbits by different writers shows great differences. Duke [1] gave the average for eighteen rabbits as 757,000 and mentioned that environmental changes cause 50 per cent variation. Bachman and his associates [27] in 127 counts on sixty-seven adult rabbits reported a maximum of 870,000 and a minimum of 450,000 platelets per cubic millimeter with an average normal variation of from 13 to 17 per cent. Petri [13] gave the average as 714,866 and Liles [18] as 375,000. Gunn [28] reported a variation of from 1,040,000 to 700,000 in young rabbits. The results obtained in this series are closest to those of Duke and of Gunn.

EFFECT OF ULTRAVIOLET LIGHT ON BLOOD COUNTS

Method.—Five albino rabbits weighing from 1,255 to 2,915 Gm. were exposed daily for periods of from three to five days at a distance of 16 inches (40 cm.). Exposures of four minutes were used as initial doses, and these doses were increased to twenty minutes in four animals and to forty minutes in two. The source of radiation was the mercury vapor quartz lamp (Victor, 110 volts, 10 amperes). Platelet, leukocyte and erythrocyte counts were made daily for periods of from five to nine days before the radiation was begun, then the animals' backs were shaved over an area about 10 by 12 cm. It was noticed that in one case an appreciable rise in the platelets followed shaving, the skin having been lacerated superficially in several places. Thereafter the backs were closely clipped with scissors, but not shaved, and counts made in each case for about five days longer to exclude this procedure as a factor. The animals, with one exception, were killed at about the time of the maximum platelet level or soon afterward.

Results.—Table 1 shows a brief summary of results in this series, and chart 1 represents graphically a typical platelet curve with ultraviolet light. Analysis of the results shows some fluctuation of the erythrocytes count which bears no definite time relationship to the experimental procedure. The leukocyte counts vary greatly, each rabbit showing at least one high leukocyte count, but the variations seem to be entirely unrelated to the experimental treatment. The temperature was not elevated during these sudden leukocytic increases; furthermore, similar increases appeared in two rabbits in the absence of any experimental procedure. Changes in temperature were insignificant at all times. The weight tended to fall slightly during the course of the irradiation.

The blood platelets showed a definite increase in number in three rabbits and no change in two. The increase percentages in R46, R48 and R49 were 163 per cent, 81 per cent and 59 per cent, respectively. The increase began in from twenty-four to seventy-two hours after the

TABLE 1.—*Influence of Ultraviolet Light on Number of Blood Platelets*

Rabbit	Weight, Gm.	Platelets			Platelet Increase, per Cent	Exposures*	Time, Min.
		Normal Average	Normal Maximum	Experimental Maximum			
46	1,710	760,000	828,000	2,000,000	163	5	5-15
47	1,625	1,062,000	1,562,000	861,000	...	3	7, 10, 15
47	2,755	792,000	913,000	984,000	24	7	7-40
48	1,918	732,000	872,000	1,323,000	81	5	8-14
49	2,915	828,000	872,000	1,316,000	59	6	6-20
54	1,255	1,619,000	2,066,000	2,105,000	..	6	10-40

* Exposures were given daily at a distance of 16 inches (40 cm.).

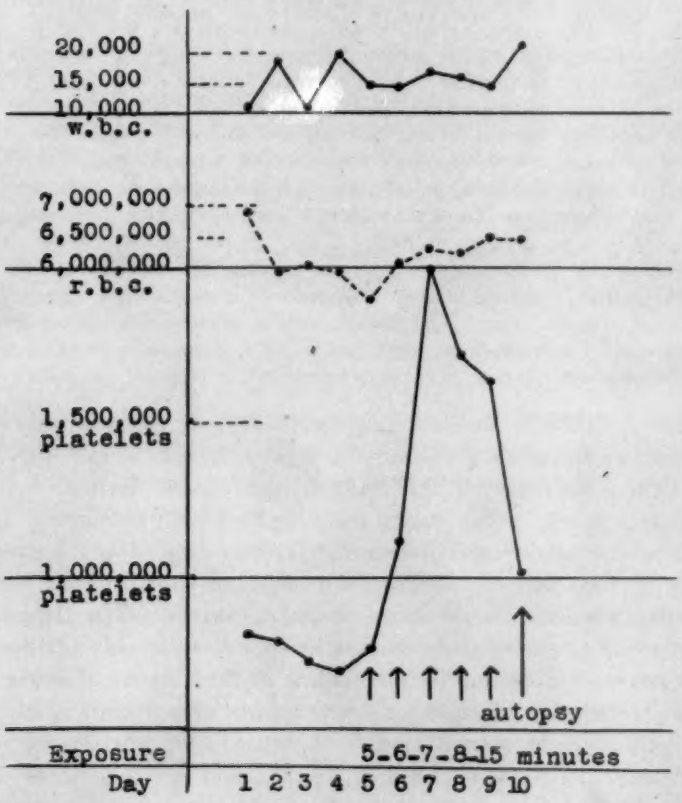


Chart 1.—Effect of exposure to ultraviolet light on platelet, red cell and white cell counts of rabbit 46.

first exposure. R47 was refractory. After one attempt to increase the platelets, the rabbit was allowed to rest for two months, after which the hair was again clipped and the procedure repeated beginning with smaller doses of radiation, which were increased to massive doses, but no significant rise was seen. R54 showed an extremely variable platelet count throughout. It was consistently high (between 1,242,000 and 2,066,000 per cubic millimeter) before radiation, and, although more stable at a higher level after irradiation, it did not rise significantly. Autopsy revealed no pathologic condition grossly.

Comment.—These results agree with those of previous investigators as to the general effects of ultraviolet light irradiation on the numbers of the blood elements, with special reference to that of the platelets. There is a rise in blood platelets following exposure to moderate doses, which begins in from one to three days, reaches a maximum within a few days, and then falls rapidly. There are rabbits, however, that do not respond to this type of stimulation. Also there are rabbits in which the daily fluctuation is normally very great. This makes it necessary to interpret all changes following experimental procedure with great caution. Furthermore, it seems that in susceptible rabbits changes can be produced with slight irritation, such as small lacerations of the skin. This must be carefully ruled out by making new normal counts after shaving or by clipping the hair instead of shaving.

EFFECT OF IODINE

The influence of iodine on blood platelets apparently has not been studied, as we have found no reference to it in the literature to the present time. Because of the wide application of iodine in surgery and its known irritating quality, a study of the effects of local applications of this drug on the blood elements seemed advisable.

Method.—Six rabbits weighing from 980 to 1,710 Gm. were used for this study. Tincture of iodine, U. S. P., was used. From one to five applications were made, at twenty-four hour intervals, to the skin of the back of each rabbit. The skin had been prepared previously by clipping the hair over areas varying in size from 7 by 10 cm. to 8 by 13 cm. Two of the animals receiving more than one application were killed at the height of the increase in platelets. The blood elements of the other four were counted until the counts were normal.

Results.—At the end of twenty-four hours, the iodine had practically disappeared from the skin. Thrombocytosis developed in four rabbits (see table 2 and chart 2) in from one to three days, which reached a maximum in a few days and then receded. In some cases, a secondary rise was observed. The return to normal was completed in about three weeks. The skin appeared normal for several days, after which erythema developed. It was not accompanied by any consistent leuko-

TABLE 2.—*Influence of Iodine* on Number of Blood Platelets*

Rabbit	Weight, Gm.	Platelets: Normal Average	Platelets: Normal Maximum	Platelets: Experimental Maximum	Platelet Increase, per Cent	Procedure
51	980	1,232,000	1,345,000	2,270,000	84	Back (8 by 10 cm.) painted on three successive days
56	1,200	1,198,000	1,349,000	1,725,000	44	Back (8 by 10 cm.) painted on five successive days
58	1,600	889,000	941,000	1,005,000	12	Back (8 by 13 cm.) painted twice
62	1,280	834,000	911,000	1,642,000	97	Back (7 by 10 cm.) painted once
64	1,710	869,000	1,107,000	1,256,000	..	Back (11 by 16 cm.) painted once
65	1,520	848,000	1,092,000	1,027,000	..	Back (10 by 15 cm.) painted once

* Tincture of iodine, U. S. P., used.

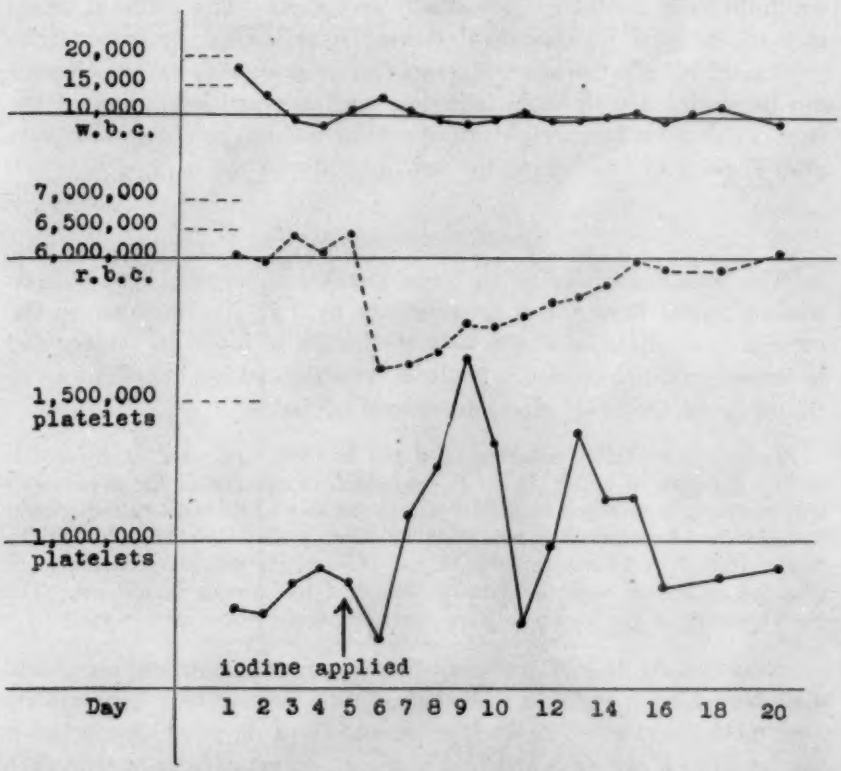


Chart 2.—Effect of external application of iodine on platelet, red cell and white cell counts of rabbit 62.

cytosis or change in temperature. The skin began to exfoliate in about two weeks. Hair grew into the new skin.

The leukocytes did not show any consistent change. Leukocytosis developed in R51 on the fourth day after three applications of iodine, but this animal was evidently sick and its temperature fell 2 F.

The erythrocytes showed a marked fall in twenty-four hours in two animals. There was then a gradual recovery completed in from two to three weeks. The other four animals showed little change in erythrocyte counts.

Comment.—Thrombocytosis developed in four of six rabbits following application of iodine to the skin of the back. In two cases, marked anemia developed in twenty-four hours. At this time, thrombocytosis had not yet developed, so that there was an actual decrease in the number of platelets present. Thrombocytosis then developed quickly. Its significance is lessened, as it was not an isolated effect. It seems probable that the secondary thrombocytosis that sometimes developed was due to the low grade dermatitis. This was slow in healing and was probably the cause of the maintenance of the thrombocytosis.

EFFECT OF COAL TAR

The effect of local applications of coal tar on the formed elements of the blood has not been previously studied. It was used in these studies principally because of its prolonged irritating effect on the skin.

Method.—Four rabbits were studied by the same method as that given for the study of the normal blood elements. Coke oven refined coal tar was applied to the skin of the back over areas from which the hair had previously been closely clipped, varying from 8 by 8 cm. to 8 by 10 cm. One application of the tar was made on each animal. All of the animals were studied until the counts of the blood elements were again normal.

Results.—There was no consistent alteration of the leukocyte counts beyond the normal variation. The erythrocyte counts, also, were not affected (see table 3 and chart 3).

Thrombocytosis developed in two animals. This occurred on the third day in one animal and on the fifth day in the other. One of these rabbits then presented thrombopenia, which lasted about two weeks. Both of the other animals showed thrombopenia, beginning on the third and sixth days and persisting in both for about two weeks. These animals had anorexia for a few days after the applications of tar, but did not have a rise in temperature. There was a slight loss in weight. The tar dried in twenty-four hours and began to peel off in a week. The hair returned.

Comment.—With the procedure used, coal tar had a variable effect on the number of blood platelets. It produced both thrombocytosis and

TABLE 3.—*Influence of Coal Tar on Number of Blood Platelets*

Rabbit	Weight, Gm.	Platelts: Normal Average	Platelts: Normal Maximum	Platelts: Experimental Maximum	Platelts: Normal Minimum	Platelts: Experimental Minimum	Platelet Change, per Cent	Procedure
59	1,070	838,000	1,090,000	1,496,000	698,000	513,000	+79	Tar applied once to area 8 by 8 cm.
60	2,020	659,000	748,000	1,245,000	563,000	646,000	+80	Tar applied once to area 8 by 8 cm.
61	1,750	1,143,000	1,233,000	1,209,000	1,001,000	686,000	—66	Tar applied twice to area 8 by 9 cm.
63	2,445	626,000	733,000	796,000	459,000	401,000	—56	Tar applied once to area 10 by 10 cm.

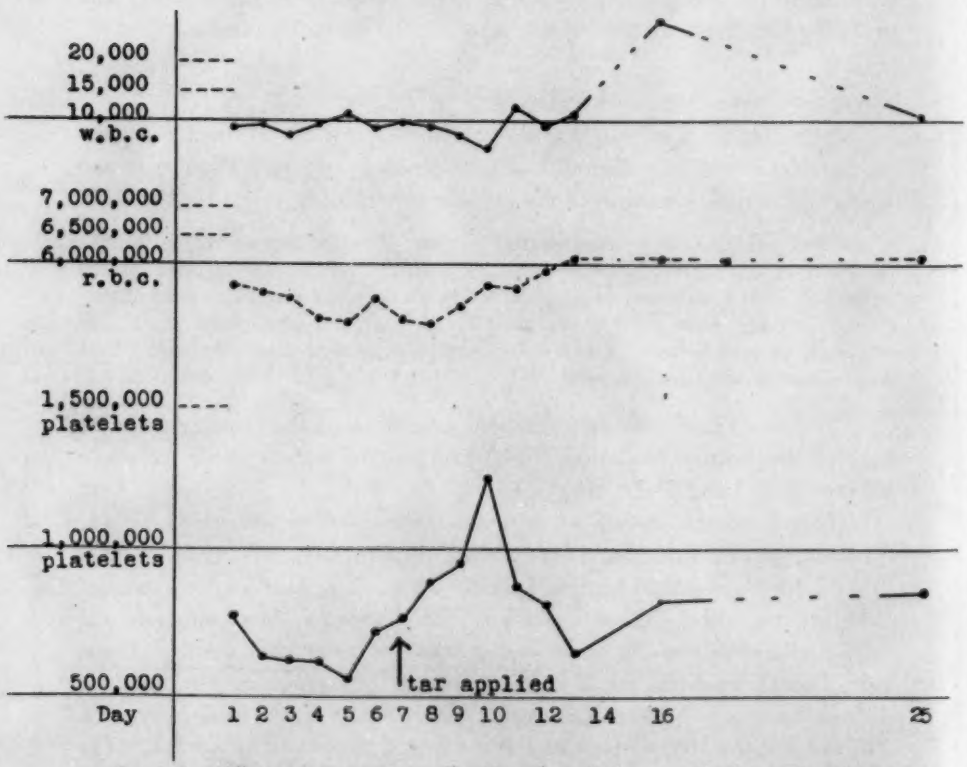


Chart 3.—Effect of external application of coal tar on platelet, red cell and white cell counts of rabbit 60.

thrombopenia. This action is like that of benzene, bacterial toxins (Duke [5]) and many other toxic substances when the dose is varied. Large doses, for this particular animal, lower, while smaller doses raise, the platelet level. There was no perceptible effect on the other blood elements.

GENERAL COMMENT

It has been shown that ultraviolet light has a rather specific effect in increasing the number of the blood platelets in the circulating blood. The action has been ascribed by Vannfalt [38] to the release of some chemical substance in the skin which has the ability to excite the bone-marrow to produce thrombocytes.

Iodine applied to the skin also increases the number of blood platelets in the circulating blood. A secondary anemia is sometimes produced, so that the thrombocytosis is not an isolated effect. The local effects of iodine are described by Sollmann: [38]

> Elementary iodine precipitates proteins, the iodine being partly adsorbed, partly loosely bound, and partly converted into iodide ions. This precipitation causes a persistent irritation, usually short of corrosion. . . . The action is chemical, since it precipitates proteins as easily dissociated compounds. . . . Elementary iodine is absorbed very effectively, but still only in very small quantity.

Coal tar has a variable effect on the blood platelets, sometimes increasing and sometimes decreasing their number. It is generally regarded as a skin irritant and produces a local erythema. Little is known about its absorbability from the skin.

The fact that all three of these agents cause local inflammation in the skin suggests that the common factor effecting alterations in platelet number might be some product of tissue injury. This would coincide with the observations of those authors who observed thrombocytosis following various operative procedures.[39]

The mechanism of the changes in the blood platelets in these experiments is not clear. Theoretically, the increases might be due either to stimulation of formation or to inhibition of destruction of the platelets. A sudden release of stored platelets from the spleen into the blood stream also occurs, but Binet and Kaplan [21] showed that such alterations are ordinarily of only about one hour's duration. The altered form of the platelets during periods of rapid increase in number suggests that there is an increase in production. Many other investigators have noted this morphologic change in experimentally produced thrombocytosis. At

---

38. Sollmann, T.: A Manual of Pharmacology, ed. 3, Philadelphia, W. B. Saunders Company, 1926, pp. 884-885 and 887.

39. Bachman and Hultgren (footnote 17). Liles (footnote 18). Dawbarn, Erlam and Evans (footnote 19).

the beginning of the rise, small, dark-staining platelets appear, many of them with one or more slender, pointed processes. They become more and more numerous until, at about the time of the maximum rise, they constitute a large percentage of the total number of platelets. The normal round or ovoid, light-staining forms then gradually replace them. The small forms give the impression of being immature, recently formed platelets. Studies have been undertaken to correlate these variations with megakaryocyte activity.

An interesting phenomenon is that no matter what the stimulus consists of or how long it is applied there is a rather definite level above which platelets will not increase in number in the circulation, and no procedure so far used has been able to prolong this high level. The maximum increases have been from about two to two and one-half times the normal. Dawbarn and his co-workers [19] have shown that the time relations of postoperative clinical thrombosis and embolism correspond exactly with those of the greatest platelet rise. This limitation phenomenon is possibly purposeful. As the origin and the fate of the blood platelets are not well understood, the mechanism in these conditions remains obscure.

SUMMARY

Ninety enumerations of the blood platelets, leukocytes and erythrocytes in the blood of fourteen normal rabbits were made. The average normal platelet counts in this group of animals were somewhat higher than those reported by other investigators.

The effect of ultraviolet light irradiation on blood platelets as reported by previous investigators was corroborated.

Iodine applied to the backs of rabbits caused thrombocytosis, beginning in from two to five days, reaching a maximum by the sixth day, and slowly receding to a normal level in from two to three weeks. Marked secondary anemia sometimes occurred within twenty-four hours, with a return of the erythrocytes to normal in from two to three weeks.

Coal tar applied to the back was followed by either thrombocytosis or thrombopenia. The numbers of the other blood elements were not appreciably changed.

The similarity between the effects on the platelet level of ultraviolet light and of other substances producing dermatitis suggests that the effects may be due to tissue injury and to the absorption of breakdown products that stimulate the formation of platelets.

THE SIGNIFICANCE OF INVASION OF BLOOD VESSELS IN ADENOMAS OF THE THYROID GLAND*

SHIELDS WARREN, M.D.
BOSTON

Although in cases of endemic goiter the adenoma-like nodules occurring in the thyroid gland cannot be differentiated from foci of abnormal involution, nevertheless certain of the more anaplastic, completely encapsulated masses may be considered as true tumors. A completely encapsulated mass found in a normal or a hyperplastic gland, and definitely varying in histologic appearance from the remainder of the thyroid gland in which it occurs, is in all probability neoplastic. The morphology of the adenomatous tissue varies widely as between individual tumors, but is fairly uniform as a rule throughout any given tumor mass. The thyroid material that I have studied, owing to geographic position, is not overrich in endemic goiter, so that the true adenomas can be fairly readily distinguished.

I have attempted to classify the adenomas into four groups according to the degree of differentiation which the adenomatous tissue shows. The papillary cystadenomas have been excluded from this study.

A growth that is made up of columns of small, closely packed cells with or without a considerable amount of stroma is considered an embryonal adenoma. This type shows little, if any, formation of alveoli, and colloid is almost never present.

The next group is slightly more differentiated. There are numerous small follicles of fetal type, often containing but a small amount or no colloid, and frequently sparsely sprinkled through an edematous stroma. This type of adenoma is peculiarly apt to undergo cystic degeneration or hemorrhage.

A third type, the simple adenoma, is made up of well differentiated thyroid tissue, often with a considerable amount of stroma, but definitely encapsulated and separated from the remainder of the gland; frequently its histologic appearance indicates a state of functional activity totally different from that of the bulk of the glandular tissue.

The fourth type, the colloid adenoma, is a completely encapsulated mass of thyroid follicles enormously distended with colloid and sharply varying in character from the remainder of the thyroid tissue.

---

* Submitted for publication, Aug. 27, 1930.

* From the Pathological Laboratory, New England Deaconess Hospital, and the Lahey Clinic.

Owing to the frequency with which these adenomas occurred, it became necessary to determine whether they were as harmless as they appeared to be, and whether any criteria could be established for determining the presence or absence of malignant tendencies.

In gross, invasion of the capsule was considered a possible evidence of malignancy, but this proved unsatisfactory for microscopic diagnosis, except in advanced cases of malignancy. It was then hoped that invasion of the lumina of blood vessels by neoplastic tissue might present the criterion desired. The value of this method of determining the malignancy of thyroid tumors, first proposed by Graham,[1] has been well established by him and others, and in some instances it is the only definite histologic criterion.

Consequently, the group of adenomas received in this laboratory from the Lahey Clinic for the five years from 1923 to 1927 inclusive were studied with a view to classification of the adenomas and to the occurrence of invasion of blood vessels. During this period a total of 1,114 adenomas was found; 34, or 3.1 per cent, showed invasion of

Adenomas of Thyroid Gland, 1923-1927

	Embryonal	Fetal	Simple	Colloid	Unclassified
Without invasion of blood vessels....	62	477	279	247	15
With invasion of blood vessels.....	5	28	0	0	1
Total.....	67	505	279	247	16

blood vessels. The table shows the distribution of the adenomas by types.

The group of unclassified adenomas is made up of those varying so widely in histologic structure that they cannot be placed in any definite group, and also those that have undergone extensive cystic degeneration, leaving little or no clue as to the type of tissue previously present.

Of the thirty-four cases showing invasion of blood vessels, thirty-two have been followed for from two and one-half to seven years. The patients who are living and well number twenty-nine. One patient died of carcinoma of the uterus without any evidence of thyroid disease. All the cases showing invasion of blood vessels occurred in women, their ages ranging from 24 to 66 years.

Two patients, or 6.3 per cent, died with multiple metastases from the thyroid tumor.

The first case, DS25-930, occurred in a woman, 28 years of age, who had had an embryonal adenoma removed on June 20, 1925, because of difficulty in breathing. The nodule was completely encapsulated. No further treatment was given. In September, 1925, a small node was

1. Graham, A.: Surg. Gynec. Obst. **42**:781, 1924.

removed from near the scar of the previous incision. This also showed the structure of embryonal adenoma. In both these tumors, a diagnosis of carcinoma could not be made either on gross or on microscopic structure, but several venules and capillaries showed definite invasion by the adenomatous tissue. The patient died on April 30, 1926, with multiple pulmonary metastases and a recurrence in the neck.

The second case, no. 38994, occurred in a woman, 29 years of age, who had had a fetal adenoma removed from the thyroid gland in 1924. In March, 1927, she reentered the hospital with a large mass in the throat and multiple pulmonary metastases. She died shortly afterward. On reexamination, the adenoma showed invasion of blood vessels.

Of 1,080 surgically removed adenomas of the thyroid gland that did not show invasion of blood vessels, none has, so far as known, given evidence of thyroid malignancy for from two and one-half to seven years after operative removal.

On the other hand, of thirty-four adenomas that showed invasion of blood vessels, two occurred in patients who died from local recurrence and multiple metastases, one in ten months and one in two and one-half years. Since 1928 postoperative x-ray treatment has been given to all patients showing evidence of invasion of blood vessels. What effect this may have it is impossible to say, but it is of interest that no patient so treated has as yet presented either a recurrence or metastases.

Graham [1] pointed out the danger which adenomas of the thyroid gland present as possible sites of origin for carcinoma. This danger is accentuated by evidence of invasion of blood vessels. Seventeen of fifty-four cases of thyroid carcinoma reported by Clute and Smith [2] apparently arose from preexisting adenomas.

SUMMARY

Of 1,114 adenomas of the thyroid gland studied, 34 showed evidence of invasion of blood vessels. Of these 34, 2 occurred in patients who died from multiple metastases. In the fatal cases, the appearance was not any more suggestive of carcinoma than in the others. A guarded prognosis should be given in those cases of thyroid adenoma that show invasion of blood vessels.

---

2. Clute, H. M., and Smith, L. W.: Cancer of the Thyroid Gland, Arch. Surg. **18**:1, 1929.

General Review

PULMONARY SYPHILIS

ITS FREQUENCY, PATHOLOGY AND ROENTGENOLOGIC APPEARANCE *

MARY C. McINTYRE, M.D.
KALAMAZOO, MICH.

Before Virchow published a detailed description of white lung of the new-born infant in 1858, Paré, Astruc and Morgagni spoke of phtisie à lué vénérea. Beyle (1810), Lagneau, Yvaren and MacCarthy (1844) attempted to draw attention to pulmonary syphilis, but their attempts failed. It was Virchow who centered attention on the subject of pulmonary syphilis, and his detailed description of the changes occurring in the lungs of the syphilitic new-born infant served as a basis for further research.

In a review of the cases of pulmonary syphilis reported between the years 1854 and 1906, sixty-five were found. Of these sixty-five cases seven were in new-born infants and fifty-eight in adults. The diagnosis of pulmonary syphilis was based on the result of antisyphilitic treatment in thirty-five cases, and in twenty-three cases the diagnosis was verified at autopsy.

The cases of syphilis of the lung in the new-born infant were reported by Lancereaux (1873), Cornil, Dubousquet-Laborderie and Gauchiers, Duzea, Fournier (1886) and Dieulafoy (1889, a). The cases of pulmonary syphilis based on the results of antisyphilitic treatment were published by Dufour, Landrieux, Lancereaux (1873), Fournier (1875, 1878), Poterin du Motel, Cube, Lutz, Schech (1882), Engel. Gaudichier, Fournier (1886), Dieulafoy (1889, b), Panas, Feulard, Thompson, Jullien, Levy, Zinn and Stengel. Those verified at autopsy were observed by Vidal de Cassis, Lancereaux (1873), Henop, Pawlinoff, Margendorff, Councilman, Delepine and Sisley, Rolleston, Lancereaux (1892), Peterson, Storch, Salomon, Zinn, Nacke, Sheib, Galvagni, Cade and Jambon, Cade and Save, Claytor and Stengel.

In this same period (between 1854 and 1906) there were thirty-eight publications other than those mentioned that dealt with pulmonary

* Submitted for publication, Dec. 26, 1930.

syphilis. These were written by Weber (1866), Moxon, Hertz, Goodhart (1874), Grandidier, Greenfield (1876, 1877), Goodhart (1877), Gowers, Green, Irvine, Pye-Smith, Tiffany, Ramdohr, Vierling, Schnitzler, Pancritius, Sokolowski, Hiller, Kroeninger, Porter, Potain (1885, 1888), Kidd, Symonds, Schech (1887), Ziemssen, Mauriac (1888), Ruhemann, MacDonald, Mauriac (1890), Perry, Satterthwaite, Hodenpyl, Marfan, Abrams, Jacquinet, Borst, Chretien, Flockemann, Hansemann, Berg, Dawson, Conner, Baumel, Hughes and Willson, Sergent (1905) and Spitzer.

In 1907 the diagnosis of pulmonary syphilis by means of the x-ray, was added to the diagnosis by therapeutic test and by the observations at autopsy. Buchanan reported the first case in which treatment was controlled by x-ray photographs. The literature between 1906 and 1920 yielded sixteen cases the diagnosis of which rested on the results of antisyphilitic treatment. These were reported by Gullan, Millian, Grindon, Roussel, Brown, Massia, Colleville, Burnham, Covisa, Culver, Hoffman, Perret, Landis and Lewis and Post.

Between 1906 and 1920 twenty-five cases of pulmonary syphilis were verified at autopsy. These were reported by Beriel, Kokawa, Koch, Osler, Henske, Shingu, Brandenburg, Sugai, Bruhl and Lyon-Caen, Fowler, Gerest and Weiss (cited by Massia) Massia, Tanaka and Robertson.

The twelve case reports published between 1906 and 1920, in which a diagnosis of pulmonary syphilis was based on x-ray evidence, were contributed by Buchanan, Massia, Blinder, Kayser (1914), Bauch, Post, Lisser and Funk. There were reports on two cases in which observations both by means of the x-rays and at autopsy were recorded. These were given by Mosny, Malloizel (cited by Massia) and by Roubier and Bouget.

Between 1906 and 1920 other papers appeared by Sergent (1908), Forsyth, Hansemann (1911), Downing, Easton, Hollman, Hays, Keilty, Potter, Wiliams, Wood, Castex and Denis, Boudet, Dexter, Leredde, Phipps, Tice, Warthin (1917), Watkins (1917), Witherspoon, Carman, Davidson and Callaway, Hall, Hoxie, Morris, Jr., Rothschild, Schonfeld, Warthin (1918), Weber (1918), Groedel, Kayser (1919), Boislineire, Carrera, Watkins (1920) Karshner and Karshner and Adelberg.

From 1920 to 1930 Bezançon and Jacob, Jacob, Letulle (1924), Howard, Letulle and Dalsace, de Jong, Benda, Fiorentini, Gautenberg, Diest, Gaté, Dechaume and Gardère, Gaté and Rousset, Koch (1929), Krohn, Vogelsang Windholz and Huguenin added reports of cases to the literature.

INCIDENCE

Letulle said: "In spite of its rarity white lung of the newborn has been described in detail and accepted while the existence of pulmonary syphilis in the adult, which according to some observers is not more rare, remains a debatable question." In 1905, Claytor found none in 13,000 specimens at the Army Medical Museum in Washington. Stanley recorded 2 cases and a doubtful one in 1,000 autopsies. The Copenhagen Hospital reported 2 in 6,000 cases, Peterson found 11 in 88 autopsies. Stolper (cited by Karshner and Karshner) found syphilitic lesions in 86 cadavers, in 61 of which the lesions were due to acquired syphilis. Of these 61 cases, 4 showed fibroid changes that were specific and 1 a gumma of the lung. Osler saw 12 cases of pulmonary syphilis in 280 autopsies, and Carrera found that 8 per cent of 152 cases showed syphilis of the lung. The Jefferson Chest Hospital (according to Karshner and Karshner) reported 4 cases in 1,200 autopsies, and Roque (according to the same authors) stated that syphilis of the lung was at least as frequent as syphilis of the liver.

AGE AND SEX

Karshner and Karshner stated that the ages ranged from 2 to 98 years. The average age was 36 years. They found the disease commonest in the early thirties. The disease affected males more than females in the ratio of 2:1, or seventy-six males to forty-two females. The number of deaths due to the disease was greater in females (twenty-one deaths in forty-two cases) than in males (thirty-one deaths in seventy-six cases).

WHITE LUNG OF THE NEW-BORN INFANT

Since white lung of the new-born infant has been the basis for research in pulmonary syphilis of the adult, a description of it will be given.

The macroscopic changes in pulmonary syphilis of the new-born infant depend on whether the lungs came from a fetus, from a new-born infant dying without having breathed or from an infant that has breathed. In the fetus and in the new-born infant that has not breathed the lungs appear augmented in volume and are pale and of firm consistence. They sink in water. In the infant that has breathed the lungs show bleached islands that stand out vividly against the red color of the normal part of the lung. The tissue is smooth, dry, nearly exsanguinated and decolorized. The lymphatics are, as a rule, hypertrophied and fibrosed. Microscopically there is a hyperplasia of fibrous tissue, accentuated in

the interlobular and interalveolar septums and in the peribronchial and perivascular tissues extending as far as the adjacent tissue beneath the pleura. All of the interstitial tissue of the lung is thickened owing to numerous fibroblasts with swollen protoplasm. These fibroblasts are fusiform in outline and have each a vividly colored nucleus that is often karyokinetic. A more or less exuberant production of elastic tissue accompanies these changes. In the midst of this connective tissue many capillaries, dilated and delimited by thickened endothelium, are seen. Plasma cells and lymphocytes are present. Around the vessels leukocytes collect in compact islands forming, at times, very small gummas (Dubousquet-Laborderie and Gauchiers, Duzea, Fournier [1886], Dieulafoy [1889, *a*]). The centers of the islands may be occupied by masses of disintegrating material (Dieulafoy [1889, *a*], Dubousquet-Laborderie and Gauchiers, Lancereaux [1873]). In this caseated mass the bronchioles and vessels are obliterated. Several of the small gummas may coalesce to form a nodular gumma with polycyclic borders.

Some alveoli disappear, while others take the form of an acinus gland as the result of stricture and subsequent dilatation. These dilated alveoli are filled with epithelium, fat and macrophages. If the desquamated epithelium predominates in the dilated alveoli, the condition corresponds to the desquamative form of Virchow.

The change in the pulmonary vessels is usually more accentuated in the pneumonic zone surrounding the gumma and consists of perivascular hyperplasia. In the arteries the muscle cells and elastic tissue disappear and are replaced by fibrous tissue. An infiltration of leukocytes occurs here and there, and these groups may reach the size of a very small miliary gumma. The lumen of the vessels is reduced, and they are lined by thickened endothelium. Obliteration may occur. Thrombo-arteritis is sometimes seen at the center of the caseating mass.

Spirochaeta pallida is always present. The spirochetes are, for the most part, in large mononuclear cells in the alveoli, but may also be seen in the bronchi, peribronchial fibrous tissue and in the epithelial protoplasm. All fibrous tissue, whether young or hyalinized, is infiltrated by them (Letulle, Virchow).

These changes in white lung of the new-born infant have formed the basis for the recognition of pulmonary syphilis in the adult.

CLASSIFICATION OF PULMONARY SYPHILIS

Karshner and Karshner divided pulmonary syphilis into (1) pneumonic forms, (2) gummatous processes, (3) syphilitic pulmonary sclerosis, (4) bronchiectasis and (5) suppurative processes, ulceration and gangrene. Howard divided it somewhat differently into (1)

gummas, (2) chronic interstitial pneumonia, (3) pulmonary sclerosis, (4) syphilitic phthisis and (5) bronchopneumonia. Krohn allowed but two forms: (1) gumma, miliary and solitary,with or without cavity, and (2) the interstitial form, which may be accompanied by bronchiectasis. Letulle gave a macroscopic classification of (1) solitary gumma, (2) massive fibrosis, (3) stellate scars and (4) islands of specific bronchopneumonia and a microscopic division of (1) "follicule elementaire" (the papule of early syphilis), (2) miliary gummas, (3) nodular gumma and (4) massive gummas.

LOCATION

In the adult pulmonary syphilis usually affects one lung, the right one more frequently than the left. The lower lobe of the right lung appears to be the site of predilection (Letulle). However, either lung or any region of either lung may be affected, even the apex, the place that earlier observers considered the site of predilection for tuberculosis. Karshner and Karshner stated that the disease begins more often in the upper lobes and spreads downward, and that at autopsy it is common to find active syphilis in the bases, with older fibrosed lesions in the right middle and upper lobes. They concluded that pathologic changes in the right lower lobe strongly suggest syphilis. In the Oxford Monograph (vol. 5) there is a statement that a primary basal lesion is presumptive evidence against tuberculosis, and that syphilis is commonly found at the hilus and base. In the cases that came to autopsy Lancereaux (1873), Mosny and Malloizel (Massia) Storch, Cade and Jambon, Duzea, Kokawa and Fiorentini found the right side involved; Henske, Beriel, Margendorff, Massia and Tanaka, the left side. The left apex and right base were found affected in the two cases reported by Gorest and Weiss (Massia). Both lungs were involved in the cases reported by Cade and Save (the exact locations were not given), Mosny and Malloizel (Massia), Roubier and Bouget, Henop, Shingu and Zinn. In the group reported by Karshner and Karshner the sites of the disease are given as follows: the right lower lobe in 68 per cent, the right upper in 55 per cent, the right middle in 43 per cent, the left upper in 36 per cent, the left lower in 36 per cent and both sides in 36 per cent. The cases diagnosed roentgenologically by Massia, Roubier and Bouget, Lisser and Funk were found to involve the right side. Bauch and Post found the left side affected and Perret, Buchanan, Mosny and Malloizel (Massia), Blinder, Massia and Funk found both sides involved. In all of these cases the sputum was negative for tubercle bacilli.

PATHOLOGY OF PULMONARY SYPHILIS IN THE ADULT

In this review the form of pulmonary syphilis given under classification will be discussed without any attempt at reclassification. The first of these is the pneumonic form.

Hiller described a gelatinous form of infiltration corresponding to the catarrhal form of Beriel. The lobe is hard and contains no air. Its color is gray or red. On section it has a homogeneous gelatinous appearance, and on pressure a viscous fluid is obtained, which is rich in cells. There is an infiltration of the alveolar walls by small cells, and the alveoli are filled with desquamated epithelium. The advanced stage shows an alveolar necrosis ending in fibrosis. Hiller believed that the infiltration was due to a compression of small pulmonary vessels by edema, or that it might be a combination of syphilitic pneumonia with ordinary pneumonia. Schnitzler thought it might be an early stage of indurative syphilitic pneumonia, but Beriel did not believe that it was specific.

In interstitial pneumonia due to syphilis the foci are well defined, fleshy and of elastic hardness. On pressure little fluid is obtained. Occasionally there are air bubbles and rarely crepitation. The lung sinks in water. Karshner and Karshner found that this type is often associated with bronchiectasis or with gumma. The connective tissue is more or less fibrosed, and microscopically the lung shows changes similar to those in white pneumonia of the new-born infant. The interstitial tissue is infiltrated by small cells, and the alveoli are smoothed out or collapsed. Other alveoli (Gaté and Rousset) are dilated and contain lymphocytes. Still others are newly formed. In places cells resembling epithelioid cells are seen. Giant cells with many nuclei, peripherally placed, may be seen, just as in tuberculosis. Small bronchi are infiltrated by lymphocytes and plasma cells. The adventitia of the vessels is thickened. Periarteritis is more common than endarteritis (Letulle). The pleura is infiltrated with the same cells and shows fibrosis of the vessels. Howard described chronic interstitial pneumonia as a diffuse infiltration in the middle lung. The lung is reddish yellow. It is smooth, airless and compact. The bronchi are sclerosed, and bronchiectasis may be associated with it. He stated that it is similar to a chronic, nonspecific pneumonia, but that it differs microscopically. Howard agreed with Warthin (1918), who stated that lymphocytes and plasma cells infiltrate blood vessels and lymphatics especially, and that there is a slight infiltration of tissue, with eventual fibrosis and atrophy or degeneration of the parenchyma. Warthin (1918) believed that the fibrosis may be directly due to syphilis, as well as to the chronic passive congestion which is present. Fiorentini stated that the fibrosis which

ensues in pulmonary syphilis cannot be differentiated from that of tuberculosis. Carrera found no pneumonic forms of pulmonary syphilis, but observed cases that responded to specific treatment.

Syphilitic bronchopneumonia was said by Letulle and Stokes to be infrequent, but Letulle stated that when islands of bronchopneumonia occur in a manifestly syphilitic lung they may be attributed to syphilis. Cavitation may occur as in tuberculosis. These islands are grayish white or grayish red and devoid of air. On section they are smooth and moist, cannot be penetrated by the finger, and show prolongations into the surrounding tissue. Some of these prolongations may reach the pleura, and at the point of contact the surface of the lung may be raised or serrated. All or almost all of the parenchymatous processes of the lung have been described as due to a bacillary caseous bronchopneumonia, but Letulle stated that syphilis may cause a process that is similar. The spirochete attacks the alveolar canals causing an exudation. The acute pneumonic focus due to the spirochete and its toxins affects alveoli, distends the interlobular acini and breaks down the interlobular septums and elastic tissue of the lung. In contrast with tuberculosis, the process almost always respects arteries and veins, but blocks the lymphatics. Caseous lymphangitis is one of the most striking traits of syphilitic bronchopneumonia (Letulle) owing to its size and volume. These islands may heal by the formation of scars or go on to cavitation. Occasionally the spirochete invades the scars causing them to break down as in tuberculosis.

If the process goes on to cavitation, the important bronchi in the caseous focus are ulcerated. Polymorphonuclear cells predominate, and fragments of elastic tissue may be seen. Even remnants of blood vessels and an isolated air space have been observed. *Spirochaeta pallida* can be demonstrated as a rule (Letulle). The cavity, when formed, shows three delimiting layers. The internal layer is jagged and friable. It is composed of granulation tissue and polymorphonuclear cells. In this layer may be found fragments of the organ, especially of blood vessels, which are recognized by the elastic tissue that is preserved in part and by the dead cells filling the lumen. Here and there elastic remnants of bronchi and alveoli may be found, if the tissue is stained especially for them. The second layer is a trellis of connective tissue and condensed granulation tissue. This may arrest the process or be included in the zone of destruction. The third layer is composed almost entirely of plasma cells and lymphocytes. It represents the zone of centrifugal expansion in which spirochetes destroy the surrounding tissue. Here the borders of one island may meet those of another. These details recall the ulcerative process of tuberculosis, with the exception that blood vessels are not attacked.

As the spirochete invades the interstitial tissue of the lung, it may create the "follicule elementaire" described by Letulle. Mononuclear cells infiltrate the septums, and the entire alveolar wall is filled with plasma cells. They usually form a double line, the rows being regular, forming a delimiting membrane. This is said never to occur in tuberculosis (Letulle).

The lobule affected by an old, fibrosed, syphilitic bronchopneumonia appears to be encased by a thick and hyperplastic tissue. The subacute, then chronic, irritation causes this excess of elastic tissue to form. The hypertrophy and hyperplasia of the epithelium of the marginal alveoli may extend to the immediately adjacent lobules. Occasionally some of the alveoli directly in contact with affected lobules show cuboidal and hyperplastic epithelium, while other alveoli remain normal or become emphysematous. While the spirochetes destroy elastic tissue, they also excite its growth, causing the excess seen in chronic cases.

The pulmonary veins in the region affected are not invaded as in tuberculosis. The latter causes a panphlebitis or thrombosis, while syphilis causes periarteritis or panarteritis (Windholz), with or without thrombosis. Infrequently the veins are attacked in a circumscribed area of the subendothelium. The mesothelium does not participate to any great extent, and the endothelium is intact. The adventitia is the site of attack. This is a point of differentiation between tuberculosis and syphilis of the lung.

The presence of a gumma may be suspected when an indurated mass is felt more or less near the pleural surface (Letulle). Karshner and Karshner found it in 50 per cent of their cases. Warthin (1918) stated:

> The gumma is not the essentially typical lesion of old or latent syphilis. It is a relatively rare formation. The essential tissue lesion of either late or latent syphilis is an irritative or inflammatory process, usually mild in degree, characterized by lymphocytic and plasma cell infiltration in the stroma, particularly about the blood vessels and lymphatics, slight tissue proliferations, eventually fibrosis, and atrophy or degeneration of the parenchyma. These mild inflammatory reactions are due to the localization in the tissues of relatively avirulent spirochetes. The pathologic diagnosis of syphilis is essentially microscopic.

On section the gumma is seen as an opaque mass with a fibrous capsule. The color varies with its age, being rose-white, whitish gray or dull yellow. It may be round or polycyclic, depending on whether it is a solitary gumma or a number of gummas that have coalesced. Its diameter varies from a few millimeters to 1 cm. or more. The consistency of a gumma depends on its age. A young, solitary gumma may be grayish red, translucent, firm and of uniform consistence. The fibrous capsule is compact and shiny and shows no anthracotic deposit.

An older gumma shows necrosis in the center and at a still more advanced stage a white, shiny, retractile, stellate scar which shows no anthracosis.

In the evolution of a gumma Letulle described four stages: (1) "follicule elementaire," (2) miliary gummas, (3) nodular gumma and (4) massive gumma.

The "follicule elementaire" is characteristic of the early stage of pulmonary syphilis and consists of spirochetes and lymphocytes. It is round, is located in the interstitial tissue and has a predilection for small bronchioles, blood vessels and interlobular and interalveolar septums. Giant cells are rarely seen, and plasma cells predominate. The venules and bronchioles appear to be immobilized by the cellular infiltration. Frequently the arterioles, venules and bronchioles in the segment in contact with the "follicule elementaire" may be infiltrated (positive chemotaxis).

The second stage in the evolution of a gumma is the formation of miliary gummas. These are spherical, contain spirochetes and vary in size. The very young miliary gumma contains leukocytes, plasma cells and lymphocytes. Often these cells are more at the periphery than at the center and in this position appear to oppose the extension of the spirochetes. In the center and at the periphery many blood vessels of varying size are seen the lumina of which are large and filled with leukocytes and erythrocytes. Lymphatic vessels are filled with leukocytes. Giant cells are rarely seen, but plasma cells and capillaries are numerous. The area of inflammation containing spirochetes is rich in collagenous fibers. The walls of the blood vessels present and newly formed are thickened. Subpleural bands may extend from the hilus to the periphery causing depressions and forming lobulations.

The gumma may heal, leaving a scar with polycyclic borders, if several gummas have coalesced, and hyaline degeneration or caseation may occur.

The central part of a caseous gumma contains granulation tissue and leukocytes undergoing karyorrhexis, and the peripheral part, fibrosis. The three zones of a gumma described by Carrera will be given later. The adjacent tissue participates in the process.

The surrounding tissue is poorly circumscribed, and beyond the lymphocytic zone are islands in which the alveoli are filled with plasma cells and lymphocytes and are edematous. Hemorrhage is rare. In places near the lymphocytic zone the interlobular and interalveolar septums are thickened, as well as the lining of the alveoli. Desquamated material fills the alveolar lumen. Around the venules and arterioles, beneath the pleura and between alveoli are lymphocytes and plasma

cells. The area of inflammation tumefies, an exudate forms, leukocytes migrate, and cells, blood vessels and lymphatics become hyperplastic. Centrifugal compression results. The alveoli and alveolar canals are compressed. The blood vessels and interlobular septums bend about the mass even to the point of distortion.

The progressive and centrifugal expansion of miliary gummas form the nodular gumma. A nodule may be found in the middle of a lobe characterized by necrosis similar to that described for miliary gummas, but it is larger and has more irregular boundaries. The nodule may be circumscribed by dense fibrous tissue, rich in plasma cells and lymphocytes, which form the zone of expansion. The same combative elements are seen in the nodular gumma that are seen in miliary gummas.

Carrera described three zones about a gumma: a central caseous area, an intermediate fibrous zone with many new blood vessels and an outer vascular, infiltrated zone rich in plasma cells and lymphocytes.

The central caseous zone presents the appearance of coarsely granular caseation in which few nuclei in varying stages of karyorrhexis are seen. The outlines of capillaries containing blood cells and fibrin can still be made out. There is no fibrin present in the caseous area except in these vessels, in contrast to the fibrin threads so abundantly found in the caseous centers of the tubercle. The intermediate zone is made up either of young fibrous tissue or of an older, more hyalin form but never distinctly epithelioid as in the tubercle. Fibroblasts appear and great numbers of angioblasts in the form of cords or young capillaries containing blood cells. The zone usually shows many plasma cells and lymphocytes and these increase in number in the outer zone, which may appear to be composed almost entirely of plasma cells, but capillary proliferation and increase of stroma can always be determined in this zone. The larger blood vessels in part show syphilitic endarteritis, particularly when the vessels appear to be the starting place of the gummatous process. Other vessels show hyalin degeneration. Many small infiltrations of lymphocytes and plasma cells with occasional endothelioid cells occur.

According to Letulle, the perigummatous pneumonia is no less specific than the gumma. New connective tissue and blood vessels are found, and bronchioles are destroyed and replaced by granulation tissue, which is thin and uniform. Only the arterioles and venules escape. The process in the surrounding areas may affect entire lobules. It is usually dotted with elementary follicles. At the onset and during the evolution of a gumma this area is moist, is rich in new blood vessels and has many fibroblasts and much collagen. After an indefinite period scar tissue forms, which is poor in blood vessels and frequently undergoes hyaline degeneration. The alveoli that have escaped are thickened, sinuous and enlarged, but are incapable of more than their normal amount of work.

Massive gummas differ from nodular gumma only in the size of the caseated area. When healed, their borders are polycyclic and send prolongations to the pleura.

Massive fibrosis, according to Letulle, is less rare than solitary gumma of the lung. It is found in the interior of the lung as coalesced islands enclosed in large cirrhotic plaques. A fine network is seen throughout the parenchyma of the lung. The connective tissue following bronchi, blood vessels and interlobular septums is thickened, radiations from the hilus are seen, and induration of the sui face of the pleura by bands of fibrous tissue cause lobulations and furrowing analogous to that seen in hepatic syphilis.

Carrera stated that a positive diagnosis of syphilis cannot be made in such cases without the typical inflammatory process due to the local action of the spirochetes, of which fibrosis is the sequel. It must be diagnosed from active areas, though certain aspects of the scar may be of aid. In a study of 152 affected lungs of syphilitic persons and 60 of persons with pulmonary tuberculosis he was unable to distinguish the fibrosis of syphilis from that of tuberculosis.

Bronchiectatic cavities were reported by Cade and Jambon, Cade and Save, Roubier and Bouget, Beriel, Brandenburg, Lancereaux (1873), Massia, Tanaka and Fowler. These bronchiectatic areas may simulate cavities. Carrera found no case of bronchiectasis, but found two cases of syphilitic peribronchitis, the essential changes in which were infiltration by plasma cells and the formation of new blood vessels. The vessels showed the typical infiltration of the intima and adventitia by plasma cells and lymphocytes. Newly formed muscle cells in connection with the bronchi were observed by him. The elastic tissue was either destroyed or displaced by the infiltration. Diest described panbronchitis in medium-sized and small bronchi resembling chronic bronchitis with bronchiectasis. Gaté, Dechaume and Gardère also found bronchiectatic cavities in their cases.

Karshner and Karshner found that pus could be squeezed from the air spaces and bronchi in lungs showing chronic bronchitis. This condition was found in 13 per cent of the cases studied. There is a dense infiltration by small cells, which, they stated, should not be confounded with miliary gummas, the latter being very dry in comparison.

Howard stated that the term syphilitic phthisis is an old one designed to include pneumonic forms, gummas, cavitation, bronchiectasis and fibrosis. Karshner and Karshner stated that a gumma may develop near the wall of a bronchus, ulcerate and empty into it, forming a cavity.

The gangrenous forms of pulmonary syphilis have not been well established. Karshner and Karshner expressed the belief that they represent a secondary infection in an ulcerated gumma or the end-result of endarteritis.

The scars of syphilis are radiating, stellate and, as far as one can judge, the remains of foci of resorbed or obliterated caseous gumma. These may occur anywhere, but more often at the base than at the apex. They are pearly white and thin. Their contiguity to injured bronchi or blood vessels, their configuration and the absence of lesions (Letulle) favor the diagnosis of an infection that acted with great intensity, had multiple foci and terminated by healing that was most destructive. In regions where parasitic infections (*Echinococcus*) are rare, tuberculosis and syphilis are the only diseases known that can produce such changes. Tuberculosis is not apt to produce such long fibrous scars centered about a resorbed caseous focus without anthracosis.

When syphilis attacks the bronchi, the spirochetes can be found in an area up to and including the epithelium the protoplasm of which is the site of predilection for the organism. The inflammatory reaction excited may be acute, subacute or chronic and may be on the inner surface of the canal or in the bronchial wall. The process may be circumscribed and isolated, just as in an artery. It may confine itself to a segment of the bronchus, reducing that portion to a small ring. The process varies in intensity. At first hyperdiapedesis and simple hyperplasia are seen. It may be confined to the epithelium, and the infiltration by plasma cells and lymphocytes may affect only the internal surface of the canal, producing a simple catarrhal inflammation with hyperplasia and desquamation. This process is essentially benign and transitory. The same process propagated along the terminal passages as far as the alveoli would cause a broncho-alveolar catarrh comparable with white lung of the new-born infant.

The ulcerative reactions in the bronchial walls are more intense and destructive. The epithelium proliferates, desquamates and almost disappears. Granulation tissue forms at the expense of the lining of the bronchi. Elastic tissue is fragmented and atrophied over large areas, and an annular band of connective tissue forms, which is rich in newly formed vessels and infiltrated by a variety of cells in which plasma cells and lymphocytes predominate. Suppuration is not extensive. On the contrary, organization of fibrous tissue takes place quickly. This organized fibrous tissue extends for some distance, encroaches on adjacent alveoli and causes mutilation of the tissue. At the periphery of this fibrous tissue the zone of invasion and centrifugal expansion is seen, and here islands of syphilitic pneumonia may occur.

Bronchi deprived, in large or small part, of their elastic tissue are said (Letulle) to be not infrequent, if a careful study is made of all cases of proved syphilis that come to autopsy. The presence of aneurysm-like segments of a bronchus should be considered as well as of those in an artery. These dilatations may follow one another in a series. These and bronchiectatic cavities should receive careful study before syphilis is ruled out. It is not inferred that any or all annular dilatations are syphilitic, but that syphilis should be borne in mind.

The ulceration may spare a few islands of tissue, 1 mm. or more in size, although the rest of the bronchial wall is seriously involved. The larger arteries are usually left intact, although the pulmonary artery has been seen to be affected (Warthin, 1917). Endarteritis and periarteritis serve to confirm the diagnosis of syphilis in certain destructive conditions of the lung. Warthin (1918) stated that the pulmonary artery is affected in the same way as the aorta.

The inflammation may go on to a chronic state. Islands of chronic bronchitis, fibrosed and atrophied, may be all that remains as a proof of the existence of syphilis.

The pleura is frequently involved in syphilitic processes of the lung (Fiorentini, Letulle). On section of a manifestly syphilitic lung, one can, with careful search, demonstrate "follicule elementaire" (Letulle) as characteristic as those in the subjacent pulmonary tissue. The serosa is filled with mononuclear cells arranged in an irregular manner along the interstices. In places one may find groups of these "follicules," and spirochetes may be demonstrated in them. Plasma cells and lymphocytes are found around blood vessels and lymphatics. The meshwork of fibrils is filled with desquamated epithelium, leukocytes and erythrocytes. The presence of spirochetes in pleural effusion has not been demonstrated satisfactorily (Letulle), but the tubercle bacillus has not always been demonstrated in effusions believed to be tuberculous.

Syphilis causes a production of new connective tissue in the pleura that is even greater than that produced by tuberculosis. This causes a thickening of the pleura. New blood vessels are seen filled with mononuclear cells. Letulle stated that caseous material has been seen to pass into the pleural space.

The scar formed in the pleura is no less characteristic than that which develops in the subjacent pulmonary tissue. In breaking down, the lung will carry some segments of the serosa deep into the parenchyma, and the subjacent lobules may become bronchiectatic. The cortical pulmonary lesions adjacent to the pleura are greater in number in pulmonary syphilis than in pulmonary tuberculosis (Letulle).

In discussing the differential diagnosis, Carrera said:

> The formed gumma and the developed tubercle can be distinguished by the vascular, more closely packed epithelioid, sharply circumscribed, conglomerating character of the latter while the gumma appears as a more loosely arranged, less sharply limited, vascular granulation tissue, scant in epithelioid and giant cells and infiltrated with lymphocytes and plasma cells. The scar of the tubercle is round, sharply delimited with concentric fibers, hyalin, scant in nuclei, devoid of vessels and elastic tissue, less given to anthracotic pigment but more frequently calcified and very often confluent and conglomerated. The scar of syphilis is irregularly radiating or stellate, not sharply delimited, more like ordinary cicatricial tissue, still contains blood vessels, often with angiectatic capillaries, continuous with the thickened walls of the nearest alveoli, still shows elastic fibers and the outlines of old vessels and alveolar walls; the scars of gummas are extremely rarely conglomerated or confluent; the syphilitic fibrosis begins under the pleura and around the bronchi and is more frequently anthracosed and very rarely calcified. But the most conclusive differential point is the finding in the fibrosis of syphilis of collections of plasma cells; and such active areas are probably as frequent in syphilitic fibrosis of the lung as they are in syphilitic processes elsewhere in the body.

Karshner and Karshner stated:

> Differentiation at the autopsy table of a gumma of the lung from similar tuberculous lesions is difficult. In favor of gumma are: 1. Location. Tuberculous nodules most commonly occur in the parenchyma. 2. Absence of calcification. Calcification is unknown in gummata of the lung. On the other hand, fatty degeneration is said to be more common in gumma. 3. Encapsulation. This is said to be a constant finding in gummata of the lung; it is more rare in tuberculosis. Microscopically the following are said to aid in diagnosis: 1. In gummata the fundamental structure of the normal tissue is said to be recognizable. 2. The presence of more or less altered blood vessels is characteristic of gumma. 3. Newly formed alveoli with cubical epithelium is mentioned more frequently in gumma than in tuberculosis. 4. Endarteritis obliterans and peri-arteritis are more common in gumma than in tuberculosis. 5. Infiltration of the small bronchi occurs more frequently in syphilis. 6. Proliferation of smooth muscle fibers is characteristic but not constant of gumma.

Koch (1929) stated that when calcification does occur in pulmonary syphilis, it is only in the gummatous form, and Gaté, Dechaume and Gardère described a case of calcified gumma. Windholz described the characteristics of pulmonary syphilis as the presence of fibroblasts at the periphery of the granulation tissue, lymphocytes, plasma cells, and obliterative bronchitis and peribronchitis. In contrast with tuberculosis, in which the caseation is of an exudative type, syphilis shows a productive reaction.

From the data contained in this paper the following points may be summarized: 1. The caseating power of syphilis is more limited than that of tuberculosis. 2. Healed tuberculosis is circumscribed, while the lesions of syphilis show prolongations. 3. Giant cells are rarer in

syphilis than in tuberculosis. 4. Plasma cells are rarer in tuberculosis than in syphilis. 5. Anthracosis is more infrequent in the scar of syphilis than in the scar of tuberculosis. Carrera believed the opposite to be true. 6. The nodule of tuberculosis may arise without a "follicule elementaire," and may begin as an island of encapsulated broncho-pneumonia. 7. The invasion of a scar with subsequent breaking down is less common in syphilis than in tuberculosis. 8. Blood vessels are more rarely attacked in syphilis. 9. The adventitia of the blood vessels is the portion that is more frequently affected in syphilis. 10. There is no epithelioid formation in syphilis as in tuberculosis. 11. The elastic tissue is better preserved in syphilitic than in tuberculous processes. 12. Syphilis produces a greater amount of connective tissue in the pleura than tuberculosis. 13. Tuberculosis does not show as many cortical pulmonary lesions adjacent to the affected pleura as syphilis.

ROENTGENOLOGIC DIAGNOSIS OF PULMONARY SYPHILIS

In 1907, Buchanan published a case of a man who, for one year, had had a condition diagnosed as tuberculosis, but in whose sputum tubercle bacilli could not be demonstrated. An x-ray film showed areas of infiltration in the bases of both lungs. These cleared up under antisyphilitic treatment. In 1910, Massia published three cases in two of which treatment was given followed by clearing up of the shadows on the film. One came to autopsy. In the latter case the x-ray photograph showed the apexes of both lungs to be involved, and at autopsy a diagnosis of white pneumonia was made, and the upper right bronchus was found to be filled with pus. Massia could demonstrate no spirochetes in the tissue. Roubier and Bouget, in 1912, reported one case in which the x-rays showed marked involvement, and at autopsy a syphilitic pneumonia was found on the right side with newly formed alveoli. In 1914, Kayser reported a case in which the shadows in the x-ray pictures cleared under antisyphilitic treatment. Two years later, Bauch reported dense fibrous bands over the entire right lung, with cavities that were probably bronchiectatic. In the same year, Lisser reported marked involvement of the cardiohepatic angle which cleared with treatment. In 1919 and 1920, Funk reported three cases. The first showed peribronchial thickening in the right lower lobe, which cleared up under antisyphilitic treatment. The second showed bilateral involvement, which cleared. The third showed an infiltration of the lower border of the upper right lobe and the upper border of the right middle lobe. In the lower lobe there was a great deal of fibrosis with possibly a bronchiectatic cavity. Others who have reported cases are Blinder, Post, Warthin (1917), Watkins (1917), Fiorentini, Diest, Krohn and Gaté and Rousset.

The x-rays establish a point of contact between the clinical observations and the results at autopsy. It may be possible to state from observation of a film where the site of the lesion is, but it is not possible to diagnose the cause definitely.

The shadows seen in an x-ray film may be due to fibrosis sufficient to arrest the rays. This fibrosis may be in the bronchi, blood vessels or interstitial tissue. Of the three sites, the bronchial is the most common.

When cardiovascular syphilis already exists and questionable shadows are seen by means of the x-rays, the question arises: Do these shadows represent bronchial fibrosis or fibrosis of the pulmonary artery? In the latter event another question presents itself: Are these shadows due to syphilis of the blood vessels, since it has been stated that syphilis respects the integrity of these structures (Letulle)? It has been stated (Letulle) that when cardiac syphilis exists, primary syphilis of the lung is ruled out as a cause for the shadows seen.

In cases of proved pulmonary syphilis, fibrosis, which has a predilection for the bronchi, if present in the pulmonary tissue, shows, in the x-ray pictures, fibrous tracts more or less serrated. These tracts radiate from the point where the main lesion is located. Large cicatricial tracts cast polycyclic shadows. The arborescent tracts are fanlike (Diest, Fiorentini, Krohn) and can be traced to their ultimate ramifications. Between these tracts are shadows due to perilobular and interlobular fibrosis. Fiorentini stated that roentgenologically the fibrosis in syphilis cannot be distinguished from that in tuberculosis, but that sclerosis localized at the hilus, calcification or cavity points to tuberculosis, and that peribronchial sclerosis with formation of rings points to syphilis.

The parenchymal shadows remain more or less circumscribed and are secondary to the sharply defined arborescent tracts. Enlargement of the mediastinal nodes or calcified nodes and annular shadows may be seen just below the hilus. These rings are probably due to fibrosis around bronchi (Fiorentini) and that portion of the bronchial tree near the median line and may occur in groups of three or four. Following the oblique direction of bronchi one may find black half circles or a more or less elliptical shadow devoid of lumen.

Arborescent tracts, diffuse fibrosis radiating in all directions from and along bronchi even to their termination, more or less marked emphysema and an enlargement about the hilus are some of the aspects of pulmonary syphilis. Even when other diseases are operating in the lung, one should not fail to look for these signs. It is not impossible that a second disease may be acting in a field already affected by syphilis.

In those cases of fibrosis in a dihybrid terrain there is frequently an extreme production of fibrous tracts (Gaté and Rousset). In some

cases calcified nodules or enlarged nodes may be seen extending from the mediastinum to the cervical region in an uninterrupted chain. (Letulle).

When the exuberant fibrous tracts join apical shadows, causing a more or less homogeneous opacity, one should consider that a fibrous tuberculosis is grafted on a syphilitic terrain and look for parahilar shadows and calcified nodules. Tuberculosis may attack the bronchi, but the shadows will be finer and the annular rings less dense than in syphilis.

Watkins (1917) stated that pulmonary syphilis must be differentiated from bronchiectasis, abscess, malignant growth, pneumonoconiosis, unresolved pneumonia and tuberculosis.

Shadows due to carcinoma will give sharp margins, while syphilis has irregular borders. Watkins (1917) believed that the absence of cavity is peculiar to syphilis, but Massia, Beriel, Storch, Cade and Jambon and Fowler reported cavity in pulmonary syphilis.

Pneumonoconiosis, according to Watkins (1917), resembles syphilis and tuberculosis combined. He also stated that no roentgenologic differentiation can be made between pulmonary syphilis and unresolved pneumonia.

As a rule, the shadows due to syphilis are in the lower and middle lobes, while those due to tuberculosis are in the upper lobes. The densest shadow in syphilis begins at the hilus and diminishes toward the periphery, while in tuberculosis the characteristic shadows are about the apical and subapical regions.

No definite points of differentiation of pulmonary syphilis from other pulmonary conditions can be given, with the exception possibly of the radiating fanlike lines seen in x-ray films, and the location, which is usually the lower lobes, more especially that on the right side.

The demonstration of spirochetes in the sputum or tissue establishes the diagnosis. While it is a routine procedure to search for tubercle bacilli, it is only in the exceptional case that spirochetes are looked for. In 1907, Koch found them in a case that came to autopsy; in 1908, Henske stated that the lung he examined was densely filled with them; in 1910, Massia reported that he had searched for them but had not found them; and in 1917, Warthin reported a case of syphilitic aneurysm of the pulmonary artery and with it the demonstration of spirochetes. In 1929, both Vogelsang and Windholz reported the presence of spirochetes.

Warthin's critical morphologic studies of syphilis and Wile's dictum that spirochetes should be searched for until found might well be applied to future research in pulmonary syphilis.

BIBLIOGRAPHY

Abrams: Report of a Case of Lung Syphilis, with Autopsy, Occidental M. Times **7**:363, 1893.

Adelberg: Tuberculosis and Syphilis, J. A. M. A. **70**:1211, 1918.

Bauch: A Report of Two Cases of Syphilis of the Lung, M. Rec. **89**:906, 1916.

Baumel: Syphilis Pulmonaire, Gaz. d. hôp. **77**:357, 1904.

Benda, R.: Le bronchite chronique syphilitique, Paris, Gaston Doin, 1927.

Berg: Pulmonary Syphilis Simulating Pulmonary Tuberculosis, M. Rec. **62**:926, 1902.

Beriel: La syphilis du poumon, Paris, G. Steinheil, 1908.

Bezançon and Jacob: Rev. de la tuberc. **4**:526, 1923.

Blinder: Syphilis of the Lungs Simulating Pulmonary Tuberculosis, M. Rec. **86**:330, 1914.

Boislineire: Syphilis Reaction of the Lung, Am. J. Syph. **4**:466, 1920.

Borst: Ueber die gegenseitige Beeinflussung von Syphilis und Tuberculose, München. med. Wchnschr. **45**:981, 1898.

Boudet: Trois observations de syphilis du poumon à forme subaigue: valeur de l'expectoration hémoptoique, Paris méd. **21**:495, 1917.

Brandenburg: Ein Beitrag zur Lungensyphilis, Beitr. z. klin. d. Tuberk. **10**:182, 1908.

Brown: Some Errors in the Diagnosis of Pulmonary Tuberculosis, Bull. Johns Hopkins Hosp. **25**:112, 1914.

Bruhl and Lyon-Caen: Foie syphilitique avec fistule broncho-biliaire, Bull. Soc. anat. de Paris, ser. 6 **2**:381, 1909.

Buchanan: Syphilis of the Lung, Brit. M. J. **1**:318, 1907.

Burnham: Syphilis of the Lung, Boston M. & S. J. **171**:411, 1914.

Cade and Jambon: Sur les lésions broncho-pulmonaire de la syphilis tertiaire, Arch. de méd. expér. et d'anat. path. **17**:649, 1905.

Cade and Save: Syphilis et dilatation bronchique, Bull. Soc. méd. d. hôp. de Lyon, Jan. 30, 1906; Lyon méd. **106**:345, 1906.

Carman: A Review of the Roentgenology of Syphilis, Am. J. Syph. **2**:325, 1918.

Carrera: A Pathologic Study of the Lungs in One Hundred and Fifty-Two Cases of Syphilis, Am. J. Syph. **4**:1, 1920.

Castex and Denis: Sifilis pulmonar, Prensa méd. argent. **3**:398, 1917.

Chretien: De l'influence réciproque des états morbides et en particulier de la syphilis et de la tuberculose, Semaine méd. **18**:89, 1898.

Claytor: Syphilis of the Lung, Am. J. M. Sc. **129**:563, 1905.

Colleville: Sur un cas de gomme syphilitique pulmonaire, La Clinique, Bruxelles **28**:353, 1914.

Conner: Syphilis of the Trachea and Bronchi, Am. J. M. Sc. **126**:957, 1903.

Cornil: Traité de la syphilis, 1879.

Councilman: Bull. Johns Hopkins Hosp. **2**:34, 1891.

Covisa: Syphilis der Lunge, Dermat. Wchnschr. **40**:81, 1915.

Cube: Ein Beitrag zur Lungensyphilis, Virchows Arch. f. path. Anat. **82**:516, 1880.

Culver: An Instance of Pulmonary Syphilis Closely Simulating Tuberculosis, J. A. M. A. **44**:355, 1915.

Davidson and Callaway: A Case of Syphilis of the Lung, U. S. Nav. M. Bull. **12**:266, 1918.

Dawson: Fibrosis of the Lung, Probably Syphilitic, Tr. M. Soc. London **25**:351, 1902.

Delepine and Sisley: Extensive Gummatous Lesions of the Liver, Diaphragm, Lung and Spleen, Tr. Path. Soc. London **42**:141, 1891.

Dexter: Pulmonary Syphilis: Report of a Case, Cleveland M. J. **16**:147, 1917.

Diest, Hellmuth: Die Lungensyphilis, Klin. Wchnschr. **1**:314, 1929.

Dieulafoy: (*a*) Syphilis du poumon et de la plèvre, Gaz. hebd. de méd. (ser. 2) **26**:285, 303, 317, 331 and 367, 1889.

(*b*) Syphilis du poumon et de la plèvre, ibid., p. 348.

Downing: Syphilis and Lung Disease, Boston M. & S. J. **172**:898, 1915.

Dubousquet-Laborderie and Gauchiers: Syphilis héréditaire tardive. Phthisie pulmonaire syphilitique guerie, Rev. de méd. Paris **4**:663, 1884.

Dufour: Union méd. du Canada **5**:798, 1868.

Duzea: Sur un cas de syphilis probablement héréditaire, Lyon méd. **59**:228, 1885.

Easton: Syphilis of the Lung, M. Rec. **88**:652, 1915.

Engel: The Diagnosis of Pulmonary Syphilis, Phila. M. Times **13**:4, 1883.

Feulard: Bull. Soc. franç. de dermat. et syph. **4**:284, 1893.

Fiorentini, Augusto: La sifilide broncopolmonaire, Policlinico (sez. med.) **35**: 606, 1928.

Flockemann: Neuere Arbeiten über Lungensyphilis, Centralbl. f. allg. Path. u. path. Anat. **10**:449, 1899.

Forsyth: Gumma of the Lung, Proc. Roy. Soc. Med. (sect. for Study of Diseases of Children) **5**:186, 1911-1912.

Fournier: Syphilis héréditaire tardive, Paris, 1886, p. 418.

De la phthisie syphilitique, Gaz. hebd. de méd. **42**:758, 773 and 802, 1875.

Phagedenesme tertiaire du pied, phthisie syphilitique, Ann. de dermat. et syph. **10**:120, 1879.

Fowler: Syphilitic Disease of the Lung, in Albutt and Rolleston: System of Medicine, New York, The Macmillan Company, 1909, vol. 5, p. 420.

Funk: Pulmonary Syphilis, Am. Rev. Tuberc. **3**:754, 1919-1920.

Galvagni, cited by Boix: Arch. gén. de méd. **191**:1314, 1903.

Gaté; Dechaume, and Gardière: Un cas de gommes miliares syphilitiques ayant réalisé le tableau clinique de la granulie, Lyon méd. **2**:235, 1929.

Gaté and Rousset: Volumineuses bronchiectasies unilatérales chez une ancienne syphilitique, Lyon méd. **2**:102, 1929.

Gaudichier: Phthisie syphalitique; guérison, Ann. de dermat. et syph. (ser. 2) **6**:152, 1885.

Gautenberg, R.: Ueber Syphilis der Lungen im Röntgenbild, Fortschr. a. d. Geb. d. Röntgenstrahlen. **37**:1134, 1928.

Goodhart: Syphilitic Disease of the Lung, Tr. Path. Soc. London **25**:31, 1873.

Phthisis of the Fibroid Form, History of Syphilis, ibid. **28**:313, 1877.

Gowers: Syphilitic Disease of the Lung, Tr. Path. Soc. London **28**:336, 1877.

Grandidier: Ueber Lungensyphilis und ihre Heilbarkeit durch die Schwefelquellen zu Nenndorf, Berl. klin. Wchnschr. **42**:195, 1875.

Green: Syphilitic Disease of the Lung, Tr. Path. Soc. London **28**:331, 1877.

Greenfield: Tr. Path. Soc. London **27**:43, 1876.

Visceral Syphilis, ibid. **28**:249, 1877.

Grindon: Pulmonary Syphilis at an Unusual Site, J. Cutan. Dis. **28**:288, 1910.

Groedel: Kardiale Stauung oder Lungensyphilis? Ein Beitrag zur Röntgendiagnostik der Lungensyphilis, München. med. Wchnschr. **66**:318, 1919.

Gullan: Syphilis of the Lung, Brit. M. J. **1**:318, 1907.

Hall: A Case of Gumma of the Entire Left Lung, Lancet **2**:779, 1918.

Hansemann: Ueber Lungensyphilis, Verhandl. d. Kong. f. inn. Med. **18**:563, 1901. Ungewöhnlicher Fall von Lungensyphilis, Berl. klin. Wchnschr. **48**:67, 1911.

Hays: Syphilis of the Lung, Laryngoscope **26**:190, 1916.

Henop: Ein Fall von luetischer Erkrankung der Lungen, Deutsches Arch. f. klin. Med. **24**:250, 1879.

Henske: Syphilitic Lobar Pneumonia, M. Fortnightly **33**:243, 1908.

Hertz: Virchows Arch. f. path. Anat. **42**:421, 1873.

Hiller: Ueber Lungensyphilis und syphilitische Phthisis, Charité-Ann. **9**:184, 1884.

Hodenpyl: Miliary Tuberculosis and Gummata Occurring in the Same Lung: Their Differential Diagnosis, M. Rec. **42**:659, 1892.

Hoffman: Syphilis of the Lung: Report of a Case, Kentucky M. J. **13**:197, 1915.

Hollman: Pulmonary Syphilis, Urol. & Cutan. Rev. **19**:181, 1915.

Howard, C. P.: Pulmonary Syphilis, Am. J. Syph. **8**:1, 1924.

Hoxie: Syphilitic Pneumonia, Southwest J. M. & S. **26**:169, 1918.

Hughes and Willson: Syphilis of the Lung Simulating Phthisis, M. News **136**: 351, 1905.

Huguenin; Foulon, and Albot: Ann. d'anat. path. **7**:108, 1930.

Irvine: Double Aneurysm of the Thoracic Aorta, Interstitial Pneumonia, Tr. Path. Soc. London **28**:63, 1877.

Jacob, P.: Rev. de la tuberc. **4**:540, 1923.

Jacquinet: Tuberculose pulmonaire chez les syphilitiques, Thèse de Paris, 1895.

De Jong, S. I.: Bronchopulmonary Syphilis, Ann. d'anat. path. **3**:194, 1926.

Jullien: Diagnostic et traitement de la syphilitis pulmonaire, Union méd. du Canada **55**:565, 1893.

Karshner and Karshner: Syphilis of the Lung, Ann. Med. **1**:371, 1920.

Kayser: Roentgenologischer Beitrag zur Klinik der Lungensyphilis, Fortschr. a. d. Geb. d. Röntgenstrahlen **22**:214, 1914.

Ueber den gegenwartigen Stand unserer Kenntnisse von der Lungensyphilis der erwachsenen, Berl. klin. Wchnschr. **56**:1733, 1919.

Keilty: Syphilis and Tuberculosis in the Same Lung, New York M. J. **104**:252, 1916.

Kidd: Diffuse Symmetrical Pulmonary Cirrhosis, Tr. Path. Soc. London **37**:126, 1886.

Koch, M.: Ueber einen Spirochätenbefund bei kavernöser Lungensyphilis und pachymeningitis hemorrhagica interna productiva, Verhandl. d. deutsch. path. Gesellsch. **10**:275, 1907.

Koch: Ueber Lungensyphilis, München. med. Wchnschr. **76**:1316, 1929.

Kokawa: Lungengummata, Arch. f. Dermat. u. Syph. **78**:319, 1906.

Kroeninger: Beobachtungen über den Befund des Auswurfes bei syphilitischer Lungenkrankung, Deutsche. med. Wchnschr. **10**:816, 1884.

Krohn, Gunther: Beitrag zur Kenntnis der Lungensyphilis, Münster Diss., 1929.

Lancereaux: Traité pratique et historique de la syphilis, 1873, pp. 203, 257, 272 and 322.
Leçons de clinique médicale faites à l'Hôpital de la Pitié et à L'Hôtel-Dieu années 1879-1891), Paris, Babé et Cie, 1892, p. 244.
Landis and Lewis: Latent Syphilitic Infections of the Lungs, Am. J. M. Sc. **150**: 195, 1915.
Landrieux: Pneumopathies syphilitiques, Thèse de Paris, 1872.
Leredde: Étude sur une forme ignorée de syphilis pulmonaire, Paris méd **20**:225, 1917.
Letulle, Maurice: Le poumon, Paris, A. Maloine et Fils, 1924.
Letulle and Dalsace: Latent Forms of Pulmonary Syphilis, Presse méd. **34**:385, 1926.
Levy: Verhandl. d. deutsch. dermat. Gesellsch., 1898, vol. 6; Arch. f. Dermat. u. Syph. **47**:414, 1899.
Lisser: Syphilis of the Lung, Am. J. M. Sc. **104**:356, 1918.
Lutz: Lungen und Rückenmarksyphilis, Aerztl, Intellegenzbl. **28**:543, 1881.

MacDonald: Pulmo-Biliary Fistula Probably Due to Syphilis; Recovery, Lancet **2**:973, 1890.
Marfan: Syphilis du poumon, Gaz. d. hôp. **65**:29, 1892.
Margendorff: Ueber Lungensyphilis, Inaug. Diss., Berlin, 1889.
Massia: Le poumon syphilitique; contribution a l'étude de la syphilis pulmonaire chez l'adulte, Thèse de Lyon, 1910-1911.
Mauriac: Syphilis tertiaire des poumons, Gaz. d. hôp. **61**:414, 1888.
Syphilis tertiaire et syphilis héréditaire, 1890, p. 436.
Milian: Syphilis du poumon, in Fournier: Traité de la syphilis, Paris, 1906.
Morris, Jr.: Pulmonary Syphilis, M. & S., St. Louis **1**:949, 1917-1918.
Moxon: A Contribution to the History of Visceral Syphilis, Guy's Hosp. Rep. **13**:329, 1868.

Nacke, cited by Flockemann.

Osler: Modern Medicine, Philadelphia, Lea & Febiger, 1907, vol. 3, p. 471.

Panas: Gommes syphilitique de l'oeil et du poumon simulant la tuberculose, Méd. mod. **2**:83, 1905.
Pancritius: Ueber die Lungensyphilis, Berlin, 1881.
Pawlinoff: Diagnose und Behandlung der Lungensyphilis, Virchows Arch. f. path. Anat. **75**:162, 1879.
Perret: Pulmonary Syphilis: Report of a Case, New Orleans M. & S. J. **69**:191, 1916-1917.
Perry, E. C.: Diffuse Syphilitic Fibrosis of the Lungs, Tr. Path. Soc. London **42**:53, 1891.
Peterson: Zur Kenntnis der Lungensyphilis, München. med. Wchnschr. **40**:725, 1893.
Phipps: Pulmonary Syphilis, with Report of a Probable Case, Boston M. & S. J. **176**:390, 1917.
Porter: Phthisis and Pneumonia in Their Relation to Syphilis, New York M. J. **42**:114, 1885.
Post: Two Cases of Syphilis of the Lung, Boston M. & S. J. **174**:876, 1916.
Potain: J. de méd. et chir. prat. **56**:15, 1885.
Syphilis et tuberculose, Gaz. d. hôp. **61**:142, 1888.

Poterin du Motel: Sur la tuberculose syphilitique, Union méd. du Canada **6**:864, 1878.

Potter: Salvarsan in the Treatment of Double Infections, Tuberculosis and Syphilis, Am. J. M. Sc. **152**:823, 1916.

Pye-Smith: Tertiary Syphilis of the Lung, Tr. Path. Soc. London **28**:334, 1877.

Ramdohr: Zur Casuistik der Lungensyphilis bei Erwachsenen, Arch. d. Heilk. **19**:410, 1878.

Robertson: Syphilis of the Lung, with Report of a Case, J. Path. & Bact. **15**:45, 1910-1911.

Rolleston, H. D.: Tr. Path. Soc. London **42**:50, 1891.

Rothschild: Ueber die Diagnose der Lungensyphilis in zweitem Stadium der Lues, Med. Klin. **65**:1199, 1918.

Roubier and Bouget: Pyopneumothorax dans la syphilis pulmonaire, Rev. de méd., Paris **32**:185, 1912.

Roussel: Pulmonary Syphilis, New York M. J. **98**:600, 1913.

Ruhemann: Ueber Lungensyphilis, Berlin, 1888.

Salomon: Bull. et mém. Soc. anat. de Paris **77**:901, 1902.

Satterthwaite: Pulmonary Syphilis in the Adult, Boston M. & S. J. **124**:573 and 600, 1891.

Schech: Lungen- und Trachealsyphilis casuistische Beitrag, Deutsches Arch. f. klin. Med. **3**:410, 1882.

Beiträge zur Lehre von der Syphilis der Lunge, Internat. klin. Rundschau, Wien, 1887, vol. 1, no. 5.

Schnitzler: Ueber Lungensyphilis und ihr Verhältnis zur Lungenschwindsucht, Wien. med. Presse **20**:14, 15, 19, 21, 27, 32, 34, 35, 38 and 41, 1879.

Schonfeld: Ueber die Röntgendiagnose bei Lungensyphilis, Med. Klin. **14**:847, 1918.

Sergent: Syphilis et tuberculose, Arch. gén. de méd. **196**:2497, 1905.

Evolution et traitement de la tuberculose chez les syphilitiques, Presse méd. **16**:657, 1908.

Sheib: Syphilis mit gummöser Affection des Magens und Darmes sowie der Lungen bei einem 51 jährigen Manne, Prag. med. Wchnschr. **25**:537 and 551, 1900.

Shingu: Zur pathologischen Anatomie multipler Lungengumma, Wien. klin. Wchnschr. **23**:971, 1910.

Sokolowski: Ueber die luetische Phthise, Deutsche. med. Wchnschr. **9**:539 and 552, 1883.

Spitzer: Ueber Spirochätenbefunde im syphilitischen Gewebe, Wien. klin. Wchnschr. **18**:822, 1905.

Stanley: Brit. M. J. **1**:181, 1911.

Stengel: Syphilis of the Lung Simulating Pulmonary Tuberculosis, Univ. Penn. M. Bull. **16**:89, 1903-1904.

Stokes: Modern Clinical Syphilology, Philadelphia, W. B. Saunders Company, 1926, p. 1068.

Storch: Beitrag zur Syphilis der Lunge, Bibliot. med., 1896, part C, no. 8.

Sugai: Ein Fall von Lungensyphilis beim Erwaschsenen, Centralbl. f. allg. Path. u. Path. Anat. **20**:193, 1909.

Symonds: Case of Syphilitic Hepatitis and Interstitial Pneumonia in an Infant, Tr. Path. Soc. London **37**:124, 1886.

Tanaka: Beiträge zur Kenntnis der Lungensyphilis beim Erwachsenen, Virchows Arch. f. path. Anat. **208**:429, 1912.

Thompson: Gumma of the Lung, M. Rec. **44**:522, 1893.

Tice: Luetic Infection of the Lungs; Pathology of Syphilis of the Respiratory Tract, M. Clin. **2**:1253, 1917.

Tiffany: Syphilis of the Lung, Am. J. M. Sc. **74**:90, 1877.

Vidal de Cassis: Traité des maladies vénériennes, ed. 2, 1852.

Vierling: Syphilis der Trachea und der Bronchien, Deutsches Arch. f. klin. Med. **21**:325, 1878.

Virchow: Ueber die Natur der constitutionell syphilitischen Affectionen, Virchows Arch. f. path. Anat. **15**:310, 1858.

Vogelsang: A Case of Syphilitic Interstitial Pneumonia, Acta dermatø-venereal **9**:411, 1929.

Warthin: Syphilitic Aneurysm of the Pulmonary Artery, with Demonstration of Spirochete, Am. J. Syph. **1**:693, 1917.
The New Pathology of Syphilis, ibid. **2**:425, 1918.

Watkins: The Roentgen Diagnosis of Lung Syphilis, Am. J. Syph. **1**:760, 1917.
X-Ray Characteristics of Lung Syphilis, J. Radiol. **1**:297, 1920.

Weber: Syphilitic Disease of the Liver, Lungs, Bronchial Glands, Dura Mater, Cranium and Sternum, Tr. Path. Soc. London **17**:152, 1866.
Syphilitic Disease of the Lungs in Adults, Clin. J. **47**:19, 1918.

Wilmans: Lungentuberculose oder Lungensyphilis? München. med. Wchnschr. **63**:1481, 1916.

Windholz, Franz: Ueber erworbene knotige Syphilis der Lunge, Virchows Arch. f. Path. Anat. **272**:76, 1929.

Witherspoon: A Case of Syphilis of the Lung with Results of Treatment as Shown by the X-Ray and Physical Signs, J. Tennessee M. A. **9**:435, 1916-1917.

Wood: Syphilis of the Lungs, Boston M. & S. J. **175**:677, 1916.

Ziemssen: Lungen-Tuberculose, Syphilis oder Carcinom, Berl. klin. Wchnschr. **24**:219, 1887.

Zinn: Ueber Lungensyphilis, Charité-Ann. **23**:236, 1898.

Notes and News

Ella Sachs Plotz Foundation for the Advancement of Scientific Investigation.—During the seventh year of this foundation 25 grants were made, 21 to scientists in other countries than the United States. Seventy-eight applications were received, 62 from foreign countries. In the seven years of its existence, the foundation has made 120 grants. In accord with the policy of aiding work on similar or related problems, investigations bearing on the general subject of nephritis have been given preference; the same is true also, but to a less extent, of work on internal secretion and infection. Applications should state the nature of the research proposed, the amount of money wanted, and the objects for which the money is to be used. Applications for grants should be sent to the secretary, Joseph C. Aub, 695 Huntington Avenue, Boston, before May 1, 1931. Walter B. Cannon is the chairman of the executive committee.

Regulation of Blood Donors in the City of New York.—In March, 1928, under the leadership of the committee on blood groups of the National Research Council, an experimental bureau was established in New York City, the main purpose of which was to supply the hospitals and private physicians in the city with properly examined blood donors.

An important secondary object was to acquire a practical experience with such a service from which could be drawn up needed regulations for the control of blood donors and donor agencies by the Board of Health.

About two years after it was started, this bureau was taken over by the Blood Transfusion Betterment Association which had been incorporated for the purpose under the auspices of the New York Academy of Medicine.

With this authority behind it, the bureau has been able greatly to extend its service without increasing its professional staff. Fifty hospitals are being served and approximately 300 donors are supplied each month.

The trustees of the Association have approved the policy of encouraging research in the bureau on all problems relating to transfusion of blood and knowledge of the blood groups.

The regulations formulated for the registration of all blood donors and for the control of donor agencies by the New York Department of Health are given in the following new sections recently added to the Sanitary Code by the Board of Health:

Section 108. Blood donors regulated; registration required; blood donor defined. No person shall act as a blood donor in the City of New York without a certificate of registration issued by the Department of Health or otherwise than in accordance with the regulations of the Board of Health.

"Blood donor" defined. The term "blood donor" as used herein shall be taken to mean and include any person who holds himself out as willing to dispose of his blood, or who offers his blood, or whose blood is used for transfusion purposes, for a fee.

Section 109. Blood donor agency. No person shall conduct, maintain or operate a blood donor agency in the City of New York without a permit therefor issued by the Board of Health or otherwise than in accordance with the terms of the said permit and the regulations of the said Board.

"Blood donor agency" defined. As used herein the term "blood donor agency" shall be taken to mean and include any office, registry, place or establishment which employs, engages or supplies or advertises or holds out to employ, engage, or supply any person or persons whose blood is or may be used for transfusion purposes.

Abstracts from Current Literature*

Experimental Pathology and Pathologic Physiology

THE INFLUENCE OF THE PERICARDIUM ON ACUTE CARDIAC DILATATION PRODUCED BY VAGAL STIMULATION. E. J. VAN LIERE and G. CRISLER, Am. J. Physiol. **94**:162, 1930.

Further evidence of the protective action of the pericardium in conditions of extreme cardiac stress was furnished by the fact that incision of the pericardium permitted greater cardiac dilatation following vagus stimulation than occurred in that circumstance in normal animals.

H. E. EGGERS.

THE EFFECT OF INSULIN ON GASTRIC SECRETION. P. F. MEYER, Klin. Wchnschr. **9**:1578, 1930.

Insulin in the chylic stomach increases the acidity and usually the volume of gastric secretion from seventy to ninety minutes after injection. The effect of insulin on the gastric secretion is an early symptom or a coincident manifestation of hypoglycemia, because the curve of the blood sugar is the inverse of that of the gastric secretion. Diabetic persons have no gastric reaction unless they become hypoglycemic. Their gastric reaction when hypoglycemic is the same, but less intense, than that of healthy persons.

AUTHOR'S SUMMARY.

THE PRODUCTION OF OSTEITIS FIBROSA BY PARATHYROID EXTRACT. H. L. JAFFE, A. BODANSKY and J. E. BLAIR, Klin. Wchnschr. **9**:1717, 1930.

The subcutaneous injection of parathyroid extract into guinea-pigs regularly produced the bone changes of osteitis fibrosa. Similar results were noted in dogs, although the changes were produced with greater difficulty.

EDWIN F. HIRSCH.

EXPERIMENTAL CHRONIC PROTEIN INTOXICATION. F. PENTIMALLI, Virchows Arch. f. path. Anat. **275**:193, 1930.

Pentimalli summarizes his experimental work previously published in Italian and discusses the significance of his observations. In view of the highly toxic action of the derivatives of heterologous proteins, when the latter are suddenly broken down within the body of the sensitized animal, Pentimalli believes it is reasonable to assume that the split products of heterologous proteins should have a toxic action when broken down more slowly over a prolonged period of time. The slow degradation of homologous proteins may be a pathogenic factor in certain human diseases. In his experimental work, Pentimalli used egg albumin, egg yolk and cow's milk, and their derivatives obtained by hydrolytic cleavage in vitro, injecting the material parenterally in small doses every day or on every alternate day into rabbits. Some of the animals died early with anaphylactic manifestations. In others, the injections could be continued over a period of months. These chronically intoxicated animals became cachectic and finally died. The most important changes noted during life occurred in the circulating blood; the most important ones seen after the death of the animals were in the tissues of the hematopoietic system. Many of the animals became anemic, especially those that received egg albumin or its derivatives. The reduction in erythrocytes was often associated with a relative lymphocytosis or monocytosis. The other proteins caused leukocytosis, the increase in the number of leukocytes being due to immature forms of the myeloid or lymphoid series. The leukocytosis was not

* All unsigned abstracts may be credited to the editorial staff.

transient; it sometimes persisted for variable periods after the injection of the foreign protein was stopped. The histologic changes in the hematopoietic tissues could be correlated with the altered blood picture.

O. T. SCHULTZ.

COMPARISON OF THE TEMPERATURES OF ANIMALS AFTER THE INJECTION OF BLOOD FROM MALARIAL AND SCARLET FEVER PATIENTS AND FROM NORMAL PERSONS. OTTO HERRMANN, Zentralbl. f. Bakteriol. **115**:145, 1930.

Herrmann injected into four rabbits and forty-five guinea-pigs, either subdurally or subcutaneously, blood from malarial patients or the blood or the brain of other animals already infected by injections from these patients. As controls, eighteen guinea-pigs were similarly given injections of blood from a normal person. Likewise, twenty-three guinea-pigs and eight rabbits were given injections of blood from patients with scarlet fever. In 70 per cent of the cases, increases in the temperature were observed in the animals given injections of blood from the malarial patients, the effects being more constant in the animals given subdural injections. The incubation period varied from four to ten days. The fevers at times lasted for a month, but they quickly disappeared following chemotherapy. Plasmodia were not found in the blood, the brain or the spleen. The animals sickened more frequently after the injection of blood from malarial patients than after injections from patients with scarlet fever.

PAUL R. CANNON.

Pathologic Anatomy

THROMBOSIS OF THE HEPATIC ARTERY. BERNARD SELIGMAN, Am. J. M. Sc. **179**:609, 1930.

Two cases of thrombosis of the hepatic artery are reported. In one, an acute case, probably secondary to an infection of the biliary tract, there was involvement of the portal and hepatic veins, a hemorrhagic infarct in the liver and thrombosis of the hepatic artery at its bifurcation, extending into the liver. In the other, a more chronic case, probably of atherosclerotic origin in a man with thrombo-angiitis obliterans, the main artery was involved, and no infarct was present. The patient probably did not die from this condition. The clinical and experimental evidence suggests that the degree of injury to the liver following occlusion of the hepatic artery depends in part on the site of the occlusion and in part on the extent of the collateral circulation.

AUTHOR'S SUMMARY.

FATAL DIABETIC ACIDOSIS. LEONA MAYER BAYER, Am. J. M. Sc. **179**:671, 1930.

Six cases of diabetic acidosis, fatal in spite of treatment, have been presented. Clinically, or at autopsy, all these cases were shown to have been complicated by an infective or gangrenous process; in one of them the diabetic syndrome developed secondary to an acute pancreatic necrosis; in one in which treatment included a huge dosage of insulin, there was exhibited an unusual nephrosis. Analysis of the records suggests that death occurred either because treatment was instituted only after intoxication had already progressed too far or because an infection inhibited the power of insulin or because the complication was itself fatal. Experiment with the use of 15 Gm. of alkali in four cases showed a significant change in the alkali level in one instance and permanent clinical benefit in none.

AUTHOR'S SUMMARY.

BRONCHOLITHS, WITH REPORT OF FOUR CASES. JOHN J. LLOYD, Am. J. M. Sc. **179**:694, 1930.

The occurrence of broncholiths was known and reported by the oldest medical observers. The stones probably originate most frequently in an obsolete tuber-

culosis of a bronchopulmonary lymph node in or near the hilus. In a fairly thorough review of the literature in the English language since 1900, reports of eighteen cases were found in addition to the reports of fifteen cases found by West in 1902. Reports of four more are added in this paper, making a total of thirty-seven. The condition probably is more frequent than reported cases would lead one to suppose, as the expectoration of stones may be easily overlooked in the taking of histories, as in case 2 reported in this paper. A calculus that by erosion has entered a bronchus may produce serious results should the stone remain in the bronchus. Perhaps such an occurrence may occasionally account for a post-hemorrhagic spread in tuberculosis as well as the production of a bronchiectasis, lung abscess or empyema.

AUTHOR'S SUMMARY.

TERTIARY SYPHILIS OF THE LIVER SIMULATING BANTI'S SYNDROME. HORACE MARSHALL KORNS, Am. J. M. Sc. **179**:811, 1930.

A case of tertiary syphilis of the liver which manifested itself as Banti's syndrome in the terminal stages is reported. The literature of tertiary syphilis of the liver reproducing the clinical features of Banti's syndrome is reviewed, from which thirty-six approved cases and thirty questionable cases are collected. One hundred and four additional cases, many of which have been cited frequently in the literature, are excluded from the category. The pathology, semeiology and treatment are discussed briefly. In particular, the great importance of applying the therapeutic test to every case of Banti's syndrome before excluding syphilis as a possible etiologic factor is reemphasized.

AUTHOR'S SUMMARY.

ANEURYSM OF THE CORONARY ARTERIES. RALPH L. COX and CHESTER D. CHRISTIE, Am. J. M. Sc. **180**:37, 1930.

A case of aneurysm of the right coronary artery is reported. There were no clinical observations suggesting this lesion. In addition to the coronary aneurysm and nodular inequalities in the circumferences of the medium-sized arteries, there were a large saccular aneurysm of the abdominal aorta and a fusiform aneurysm of the right common iliac artery. There was an extreme degree of sclerosis of the coronary arteries, with occlusion of the left ramus descendens and extensive myocardial infarction. This is the thirty-first instance of aneurysm of the coronary arteries that we have found reported in the literature.

AUTHORS' SUMMARY.

LIPOMA OF THE MEDIASTINUM. WALLACE M. YATER and E. STUART LYDDANE, Am. J. M. Sc. **180**:79, 1930.

Lipoma of the mediastinum is rare, only twelve cases, including the one described in this report, having been recorded as far as could be ascertained. In only one instance was the tumor confined to the mediastinum. In the others, it had grown externally either upward into the neck or through an intercostal space or defect of the sternum to form a tumor of the chest wall, or it had forced its way into one or both sides of the thoracic cavity. Symptoms due to pressure were noted in only four cases. In the case reported here, moderate dyspnea on exertion had been present for eleven years, and the patient died of lobar pneumonia. The lipoma weighed 8¼ pounds (4.1 Kg.) and filled the anterior mediastinum, the precordium and the lower two thirds of the right thoracic cavity.

AUTHORS' SUMMARY.

MULTIPLE ANEURYSMS OF THE ARTERIES OF THE RIGHT ARM ASSOCIATED WITH ARTERIOVENOUS FISTULA AND ARTERIAL EMBOLISM. DWIGHT L. WILBUR, Am. J. M. Sc. **180**:221, 1930.

The association of multiple aneurysms of the right brachial, radial, superficial palmar, common volar digital and volar digital arteries with an embolus in

the radial artery and an arteriovenous fistula of the hand is recorded. This combination of changes is of unusual interest to the physician because of its rarity and because of the many fields that it opens for investigation, and to the surgeon because of the many difficult therapeutic problems that it presents.

AUTHOR'S SUMMARY.

UNINFECTED MURAL THROMBI OF THE HEART. EARLE A. HARVEY and SAMUEL A. LEVINE, Am. J. M. Sc. **180**:365, 1930.

Uninfected antemortem mural thrombi of the heart were found in 5.3 per cent of all necropsies at the Peter Bent Brigham Hospital. Cardiac mural thrombi were twice as frequent in males as in females. The majority of these patients died between the ages of 40 and 70 years. The patients with ventricular thrombi following cardiac infarction formed the group of greatest age (62 years). There was a large middle-aged group with valvular disease (45 years). The frequencies of the sites of formation of single mural thrombi were: left ventricle, 31; right auricle, 28; left auricle, 6, and right ventricle, 4. There were forty-two cases of multiple thrombosis. The apexes of the ventricles and the auricular appendages were the most frequent sites of formation of mural thrombi. Secondary infarction outside the heart as a result of emboli occurred with the following frequencies: pulmonary, 47; renal, 18; splenic, 12, and cerebral, 3 (the brain was examined in only a limited number of instances). There were six instances of peripheral arterial thrombosis that may have been embolic. Auricular fibrillation definitely increases the incidence of auricular thrombosis. The two most frequent mechanisms for the formation of cardiac mural thrombi are the myocardial degeneration associated with coronary arterial disease and the improper functioning of the auricles leading to blood stasis. The diagnosis of cardiac mural thrombosis presents difficulties, but this condition should be suspected in cases of coronary thrombosis and chronic valvular disease showing evidence of emboli.

AUTHORS' SUMMARY.

THE MUSCULONERVOUS STRUCTURES IN THE SUBMUCOSA OF THE APPENDIX. P. MASSON, Am. J. Path. **6**:217, 1930.

The submucosa of the normal appendix contains muscle bundles, continuous, on the one hand, with those of the circular muscle, and on the other hand, with those of the muscularis mucosae. These two muscle groups often anastomose in the middle zone of the submucosa. They are in intimate relation with certain parts of Meissner's plexus. Muscle and nerve together form a complex which may be termed the musculonervous complex of the appendicular submucosa. Under influences that cannot yet be defined, but that are connected, no doubt, with inflammatory crises, the muscle bundles and the nerves become more numerous, acquire more and more intimate relations, and by their accumulation contribute to the thickening of the submucosa. At the same time, the arteries enlarge, their muscle coat hypertrophies, and the arterial nerves become more prominent. The mucosa presents certain changes which in the order of frequency are: decrease in number or complete absence of lymph nodules, scarcity of lymphocytes in the stroma and diffuse hyperplasia of its nerve plexus, to which may be added more localized hyperplasias in the form of ill-defined neuromas or circumscribed neuromas situated in the middle or upper part of the mucosa. In extreme examples there is, in addition, hypertrophy or hyperplasia of the muscle coat and of Auerbach's plexus. To sum up, there are hyperplasia and hypertrophy either of the sympathetic nerves or of the appendicular muscles, or of both, in other words of the motor apparatus of the appendix, together with atrophy of the lymphoid tissue. This series of lesions seems to begin by the formation of these musculonervous complexes.

AUTHOR'S SUMMARY.

MULTIPLE INTRACRANIAL ANGIOMAS. KIYOSHI HOSOI, Am. J. Path. **6**:235, 1930.

A case of multiple intracranial angiomas associated with multiple intracranial meningiomas all on the right side is reported, with the observations at autopsy. The patient presented no symptoms or signs of definite cerebral localization. The literature on the subject is briefly reviewed.

AUTHOR'S SUMMARY.

MENINGIOMAS (MULTIPLE INTRACRANIAL TYPE). KIYOSHI HOSOI, Am. J. Path. **6**:245, 1930.

Two cases of cranial meningioma are here presented: one of multiple dural meningiomas associated with multiple angiomas of the cerebral cortex; and the other, a solitary meningioma with hyperostosis cranei. The tumor cells of the meningioma are mesodermal in origin. They elaborate reticulum, fibroglia, collagen and elastic fibrils. The multiplicity of the intracranial meningiomas and angiomas in case 1 connotes a marked disturbance of the mesodermal germ layer. Clinically and histologically, the meningiomas in these two cases indicate a long drawn-out course. In consideration of the large size attained by these growths, it is remarkable that a tumor of the brain was not suspected. The first case was thought to be a mental case due to the patient's frequent depressive states associated with fits of crying. The second patient, who was under the constant care of a neurologist, was being treated for idiopathic epilepsy. The brain tissue immediately surrounding the meningiomas and the angiomas and also far removed from these growths showed no reactive increase in microglia or oligodendroglia, although in the adjacent cerebral cortex in both cases, so-called "amyloid" bodies were abundant. A reactive gliosis was present in the tissue adjacent to the ventricular tumor.

AUTHOR'S SUMMARY.

NEPHROSIS IN MULTIPLE MYELOMA. DAVID PERLA and LAURENCE HUTNER, Am. J. Path. **6**:285, 1930.

Two instances of multiple myeloma with severe nephrosis and shrinkage of the kidney are reported. A review of the literature reveals several other similar instances. A study of the pathologic changes of the kidneys in instances of multiple myeloma associated with Bence-Jones albumosuria is made. From this analysis it is concluded that the pathologic changes found in the kidney in multiple myeloma consist of three distinct elements, no one of which is constantly present but all three of which may be present: a nephrosis specifically associated in some way with the Bence-Jones albumosuria and the myeloma; arteriosclerosis of the kidney, an independent vascular disease of the kidneys, present in a milder or severer form in almost every instance of multiple myeloma occurring in the age group of from 50 to 70 years, and calcium deposits in the kidney tubules dependent on a destruction of bone and the release of large quantities of calcium in the blood. Clinically, the nephrosis differs from the idiopathic type in the absence of edema, in the increase in the concentration of nonprotein nitrogen in the serum and in the inability to concentrate urine, with a consequently low specific gravity of the urine. Anatomically, the nephrosis is severe and the kidneys are contracted. The kidneys are small and pale with smooth surface and markedly narrowed cortex. Microscopically there is extensive destruction of the tubules of the cortex and medulla, with replacement by dense cellular fibrous tissue. Though there is some hyalinization of a few glomeruli, this lesion is apparently associated with a concomitant arteriosclerosis, the primary lesion being the destruction of the tubules.

AUTHORS' SUMMARY.

HISTOLOGICAL CHANGES IN THE RENAL GLOMERULUS IN ESSENTIAL HYPERTENSION. LEONE MCGREGOR, Am. J. Path. **6**:347, 1930.

The glomerular lesion of essential hypertension is as typical as the arteriolar lesion. It consists of a decrease in size and a simplification of the glomerulus,

with a marked thickening and wrinkling of the glomerular basement membrane. In this series of fifty-one cases, the average percentage of such glomeruli is 47 in the renal group (death from uremia), 33 in the cardiac group (death from myocardial insufficiency or coronary disease) and 24 in the cerebral group (death from apoplexy). The arteriolosclerosis precedes, and is related to the change in the glomerular basement membrane. Kidneys from persons dying in the fifth, sixth, seventh and eighth decades with a history of normal blood pressure show 96.2 per cent normal glomeruli. A rare hypertensive contracted glomerulus may be found. There are inflammatory glomeruli in any type of essential hypertension, but they are most numerous in the renal group. The lesions are usually focal, and as many as 15 per cent of the glomeruli may be involved. Aniline blue (Mallory-Heidenhairn azan carmine) is recommended as a routine stain for kidney tissue. It is particularly helpful to differentiate the renal group of cases of essential hypertension from cases of chronic glomerulonephritis that present extensive vascular disease.

AUTHOR'S SUMMARY.

A CASE OF LYMPHOBLASTOMA, HODGKIN'S DISEASE AND TUBERCULOSIS. H. E. MACMAHON and F. PARKER, JR., Am. J. Path. **6**:367, 1930.

A case is described of an elderly patient who was admitted to the hospital with the diagnosis of aleukemic leukemia. He was watched over a period of three years, and during that time a manifest lymphatic leukemia developed. Following a short but severe infection, his white blood count and differential values returned to normal and remained unchanged till his death a year and a half later. Autopsy showed that he had not only aleukemic leukemia, but also Hodgkin's disease and generalized tuberculosis.

AUTHORS' SUMMARY.

MARKED DILATATION OF THE LEFT AURICLE OF THE HEART. E. A. BURKHARDT, JR., Am. J. Path. **6**:463, 1930.

The auricular dilatation described is associated with mitral stenosis of rheumatic origin. Many cases show more marked mitral stenosis with little or no auricular dilatation. Emanuel expressed a belief that the auricular dilatation is due to auricular myocardial damage. To prove this point he described a heart in St. Bartholomew's Hospital Museum, the left auricle of which is markedly dilated yet the mitral valve of which admits three fingers. A heart in the University College Hospital is similar, the mitral valve of which is only slightly thickened. Bach and Keith presented a heart with marked left auricular dilatation, the mitral valve of which admits three fingers. This case, however, as most cases cited in the literature, presents pericarditis with the valvular lesions. This reaction is symbolic of a pancarditis that includes the myocardium of the left auricle. Increased intra-auricular pressure through an incompetent mitral valve plus a damaged myocardium probably accounts for marked left auricular dilatation.

AUTHOR'S SUMMARY.

HISTOLOGICAL STUDIES ON THE BRAIN OF A CRANIOPAGUS. K. LÖWENBERG, Am. J. Path. **6**:469, 1930.

The case described belongs in the group of craniopagus parietalis. The malformation is confined to the skull and brain. The brain of the child "A" is asymmetrical and shows pronounced malformation of the gyri and sulci, which makes the identification of the latter difficult. Many sulci are absent. The general outlines of the brain are like those in a 7 or 8 months old fetus. Histologically, both the granular and the agranular six-layer types of cortex are present. In the precentral region, the fourth layer is still granular in structure, which corresponds to the development of the eighth month of intra-uterine life.

AUTHOR'S SUMMARY.

CONGENITAL ANEURYSM OF THE INTERVENTRICULAR SEPTUM. D. E. CANNELL, Am. J. Path. **6**:477, 1930.

The clinical and pathologic observations in two cases of congenital aneurysm of the interventricular septum are here reported. The absence of clinical signs and symptoms in both cases, wherein marked distortion of the normal anatomy was present, is remarkable. A critical study of these cases adds further evidence in favor of these anomalies being congenital malformations, rather than the terminal results of endocarditis.

AUTHOR'S SUMMARY.

RENAL LESIONS WITH RETENTION OF NITROGENOUS PRODUCTS PRODUCED BY MASSIVE DOSES OF IRRADIATED ERGOSTEROL. TOM DOUGLAS SPIES and EUGENE C. GLOVER, Am. J. Path. **6**:485, 1930.

The administration of massive doses of viosterol to rabbits caused marked histologic changes in the kidneys. The chief changes were sclerosis and hyalinization of the walls of blood vessels, and thickening of the basement membranes of the tubules and glomerular capsules, accompanied in both by extensive subepithelial deposits of hyalin. There was abundant deposition of calcium in these localities. Pronounced atrophy of the tubular epithelium also occurred. The lesions were accompanied by the appearance of large amounts of albumin in the urine and by retention of nitrogenous products in the blood. The degree of nitrogen retention was in general proportional to the amount of damage of the kidney, as evidenced by histologic examination.

AUTHORS' SUMMARY.

METASTASIZING "CARCINOID" TUMOR OF JEJUNUM. ISTVAN GASPAR, Am. J. Path. **6**:515, 1930.

A case of multiple carcinoid tumors of the jejunum, one of which caused intestinal obstruction, with metastases in the mesentery and liver, is reported. Histologic examination revealed the picture of typical carcinoid tumor. Serial sections definitely indicate that at least two of the tumors originated in the crypts of Lieberkühn. Positive silver impregnation of the tumor cells confirms Masson's contention that the origin of carcinoid tumors is in the Nicholas-Kulchitzky-Masson cells in the glands of Lieberkühn. Carcinoid tumors may assume clinical significance.

AUTHOR'S SUMMARY.

SMALL CELL CARCINOMAS OF THE LUNG. HOWARD T. KARSNER and OTTO SAPHIR, Am. J. Path. **6**:553, 1930.

Small cell primary tumors of the lungs or bronchi are epithelial in character, as indicated by cell arrangement, relation of connective tissues and blood vessels and complete absence of capacity to form reticulum. Small cell cancers of the lung originate in bronchi of bronchioles and are probably unicentric in origin. Small cell cancers of the lung more frequently produce large mediastinal masses than do other cancers of this organ and are firmer in consistency, but in other clinical and gross pathologic aspects show no distinctive characters.

AUTHORS' SUMMARY.

MULTIPLE GUMMAS OF THE HEART IN THE NEW BORN. JOHN W. WILLIAMS, Am. J. Path. **6**:573, 1930.

A case of gumma of the heart in a Negro infant that died a few hours after birth is reported. The term gumma as descriptive of the lesion is questioned, since the microscopic picture is at variance with that of gumma. The terms "localized syphilitic cellulitis" and "fulminative syphilitic myositis" are suggested in its stead as descriptive of this lesion, since it is characterized by destruction of muscle and infiltration with lymphocytes, polymorphonuclear leukocytes, monocytes and plasma cells.

AUTHOR'S SUMMARY.

MULTILOCULAR CYST OF THE SPLEEN PRODUCED BY INFARCTS. W. DOBRZANIECKI, Ann. Surg. **92**:67, 1930.

Cysts of the spleen may be of the dermoid type, or they may have their origin from inclusions of peritoneum that undergo secondary degeneration; in other instances, the dilated spaces have been shown to be of lymphatic derivation. Previous abscesses, inflammatory processes about the spleen and trauma have been the causative factors in some cases. The author reports the occurrence, in a woman, aged 38, of a cyst of the spleen, measuring 25 by 13 by 14 cm., which contained 140 cc. of amber-colored, transparent fluid that coagulated after removal. He attributes the process to obliterative endarteritis, with necrosis and infarction, as the result of emboli.

RICHARD A. LIFVENDAHL.

ACUTE ULCERATION OF THE STOMACH IN CHILDREN. B. R. SHORE, Ann. Surg. **92**:234, 1930.

The literature of the subject is reviewed and the following case reported. The posterior fundic wall showed a perforation 3 cm. wide, which represented an ulcer that had penetrated. The ulcer was characterized by necrotic edges in which the submucosa and the muscularis were swollen and edematous and showed thrombosed vessels. The abdominal cavity contained free air and fluid. For several days previous to the perforation the child had had a "running nose," but there was also a history of its having swallowed some broken glass at the age of 22 months. The glass, however, was not found at operation or at autopsy.

RICHARD A. LIFVENDAHL.

INTRA-ARTICULAR ENDOTHELIAL TUMORS ARISING FROM SYNOVIAL MEMBRANE. L. C. WAGNER, Ann. Surg. **92**:421, 1930.

From the knee of a man, 35 years old, a hard, encapsulated, yellowish-brown tumor, 7 by 5 by 3 cm., was removed, which had the gross appearances of a fibroma, but which microscopically was regarded as a fibro-endothelioma, most likely arising from the endothelial cells lining the bursa. Although treatments with the x-rays and Coley's toxin were given, local recurrences were present within two years, necessitating a midthigh amputation. A second case of intra-articular endothelial tumor arising from the synovial membrane occurred in the ankle joint of a girl 15 years of age. These 2 cases represent the only ones in 467 explorations of major joints of the body.

RICHARD A. LIFVENDAHL.

MULTIPLE MYELOMA AS A SINGLE LESION. C. F. GESCHICKTER, Ann. Surg. **92**:425, 1930.

The two cases of multiple myeloma as a single lesion reported substantiate the claim for consideration of multiple myeloma in the differential diagnosis of single lesions of bone; one occurred in the femur and the other in the clavicle. In the former, no other bones were involved at the time of writing; no Bence-Jones protein was found in the urine; there was no lumbar backache with signs of early paraplegia; the hemoglobin and erythrocyte determinations were normal, and there were no evidences of nephritis with nitrogenous retention. Thus, the six cardinal diagnostic points were violated. Giant cell tumors, metastatic carcinoma, chloroma and myxochondroma were considered in the differential diagnosis.

RICHARD A. LIFVENDAHL.

GASTRIC SEQUELAE OF CORROSIVE POISONING. WILLIAM S. BOIKAN and HARRY A. SINGER, Arch. Int. Med. **46**:342, 1930.

The ingestion of acid, even in relatively small quantities or low concentrations, may be followed by stenosis of some part of the stomach without esophageal

involvement. The swallowing of lye leads to esophageal obstruction associated frequently with gastric obstruction, rarely to gastric obstruction alone. Organic obstruction of the stomach does not occur immediately, but usually manifests itself several weeks after the recovery from the initial effects has been considered complete. Late gastric stenosis should be anticipated in all cases of corrosive ingestion (especially when the substance is known to be an acid), even though the patient is restored to complete health shortly after the poisoning. The type and location of the lesion in the upper part of the gastro-intestinal tract can be predicted from a knowledge of the corrosive ingested, whether acid or alkali, and the state of the stomach, whether empty or full. In late cases of cicatricial stenosis of the stomach, gastro-enterostomy is the operation of choice. In early cases in which an active inflammation exists, a preliminary jejunostomy is often advisable.

AUTHORS' SUMMARY.

SPONTANEOUS RUPTURE OF THE NORMAL SPLEEN. W. H. BYFORD, Arch. Surg. **20**:232, 1930.

A search of the literature revealed eight cases of spontaneous rupture of the normal spleen. The symptoms are those of severe abdominal pain followed by shock, evidences of hemorrhage, pain radiating to the shoulders, and tenderness and vomiting, therefore similar in every respect to traumatic rupture of the spleen, with the absence of the traumatic etiology. The spleen in the reported case weighed 156 Gm. and measured 17 by 18 by 2 cm. Much of the hemorrhage was subcapsular. The microscopic section failed to reveal any pathologic change in the parenchyma. The author reviews the various theories, most of which hold a diseased spleen to be the primary factor. The author, however, feels that spontaneous rupture of the normal spleen occurs.

N. ENZER.

CONGENITAL CYSTIC LUNG. IRVING J. WOLMAN, Bull. Ayer Clin. Lab. of Pennsylvania Hosp., 1930, no. 12, p. 49.

A case of congenital cystic lung in a six months' stillborn fetus, discovered in the course of a routine necropsy, is recorded. The author holds that the cystically dilated intercommunicating bronchioles and aveoli form a closed system, or systems of chambers, not continuous with the main bronchi.

METAPLASIA IN THE LYMPH NODES AND SPLEEN IN A CASE OF MYELOGENOUS LEUKEMIA. WEBB HAYMAKER, Bull. Ayer Clin. Lab. of Pennsylvania Hosp., 1930, no. 12, p. 55.

A case of leukemia is described in which there was marked extramedullary hematopoiesis. The relative aplasia of the bone-marrow, particularly in the formation of erythrocytes, together with the numerous islands of developing erythroblasts and granuloblasts in the spleen and lymph nodes, leads to the assumption that these organs had returned to their embryonic function of producing myeloid cells. Further evidences supporting the view of metaplasia and opposing that of mere colonization were: the size and the homogeneity of the spleen and the absence of clumps of myeloid cells in other organs.

AUTHOR'S SUMMARY.

HISTOLOGICAL CHANGES IN NERVE CELLS FOLLOWING INJURY. ORTHELLO R. LANGWORTHY, Bull. Johns Hopkins Hosp. **47**:11, 1930.

The nerve cell injuries that are discussed here involve both the nucleus and the cytoplasm. The nucleolus is considered to be very resistant, but a marked swelling of this structure may be seen in the cells. When death occurs immediately from electrical injuries, many of the cells have nuclei that are shrunken and that stain a uniform deep color, so that nucleolus and chromatin strands may no longer be distinguished. The nucleus is often displaced to one side of the cytoplasm and

is surrounded by a pale area indicating its former size. The suggestion is made that cells with deep-staining shrunken nuclei have no longer the power of recovery. Abnormalities following less severe damage of the nerve cell are illustrated. The cytoplasm of the injured cells is shrunken, and the perivascular space is large. Immediately following the trauma, there is a considerable decrease in Nissl substance, and that which remains has lost its flaky appearance and looks coarsely granular. Often the edges of the cytoplasm appear to have no continuity, as if the cell had ruptured into the perivascular space. Swelling of the nucleolus occurs. A few hours after the electric shock the whole cytoplasm stains a uniform, deep color and no granules may be found. The Nissl substance is gradually reformed over a period of days, sometimes appearing first in the periphery of the cell and sometimes in the center around the nucleus. Restitution of the nucleus takes a longer time. Cells that are injured beyond possibility of recovery become greatly shrunken, and cytoplasm and nucleus stain a uniform black color. Such cells are removed by phagocytosis. The electrical current has a selective effect on the nerve cells; some anterior horn cells are greatly injured while others are fairly normal.

AUTHOR'S SUMMARY.

THE PLACENTA FROM A CASE OF MALARIA. GEORGE B. WISLOCKI, Bull. Johns Hopkins Hosp. **47**:157, 1930.

The study of the placenta in a case of malaria affords proof that the chorionic syncytium is incapable of phagocytosing an inert suspension of pigment present in the intervillous spaces or of transmitting such particles from mother to fetus. Malarial parasites are present in the placenta in great abundance within the erythrocytes in the intervillous spaces. Malaria induces the accumulation of large numbers of monocytes and lymphocytes in the placental circulation. Of these cells, the monocytes phagocytose, abundantly, pigment released by the activity of the malarial organisms. These phagocytic monocytes do not penetrate the fetal tissues, but enter the masses of fibrin formed on the villi, which are denuded of syncytium at these sites. Typical clasmatocytes are not encountered in the intervillous spaces. The monocytes and lymphocytes that gather in the placenta are brought there from other parts of the maternal body where they are produced. The villi, including their stroma and covering chorionic syncytium, are anatomically normal and not visibly affected by the malarial organisms or by their products. It is unlikely that malarial organisms can enter or penetrate the chorionic syncytium, so that the transmission of malaria from mother to fetus occurs rarely, if at all.

AUTHOR'S SUMMARY.

ANASTOMOSIS OF THE HEPATIC AND PORTAL CIRCULATIONS. JOHN MCKEE OLDS and EDWARD STEPHENS STAFFORD, Bull. Johns Hopkins Hosp. **47**:176, 1930.

The hepatic artery communicates by means of capillaries directly with the sinusoids of the liver lobule at the periphery of the lobule. The portal vein also communicates directly with the hepatic sinusoids at the periphery of the lobule. There are no interlobular capillary anastomoses between the hepatic artery and the portal vein. The capillaries of the bile duct plexuses (branches of the hepatic artery) communicate directly with the hepatic sinusoids at the periphery of the lobule. No translobular arteries can be demonstrated. Mixing of hepatic arterial and portal venous blood occurs via the outermost or peripheral sinusoidal anastomoses, but not within the interlobular tissue itself.

AUTHORS' SUMMARY.

ASBESTOSIS BODIES IN SPUTUM AND LUNG. K. M. LYNCH and W. A. SMITH, J. A. M. A. **95**:659, 1930.

In microscopic sections of lung from the body of a worker in an asbestos factory, who died from a gunshot wound, numerous asbestosis bodies were found

in the alveoli, the walls of the alveoli, the deeper pleural tissues, the bronchi, and the interlobular framework, in thrombi in the veins and in the peribronchial lymph glands. Associated with them were black granular pigment, in the lymph glands a yellow-brown granular substance, a reaction of mononuclear and polymorphonuclear giant cell phagocytes and in the framework structures a cellular increase in fibrous tissue. The asbestosis bodies were seen in the sputum of three people who had been workers, in an asbestos factory, one as long before as six years. In the sputum, these bodies had a central filament of a transparent, slightly greenish-tinged, needle-like crystal. On this were deposited nodules, blebs and segments of a homogeneous refractive substance. These bodies were from 12 to 140 microns long and from 1 to 12 microns thick. They did not take the ordinary dyes for tissue and sputum. They could be stained by the prussian blue reaction for iron. It is suggested that the iron content of the deposit was of tissue origin, probably from the blood.

GEORGE RUKSTINAT.

INTRANUCLEAR BODIES IN RENAL DISEASE OF CALVES. THEOBALD SMITH, J. Exper. Med. **51**:519, 1930.

Renal lesions chiefly the result of obstructive processes were associated with intranuclear bodies in the epithelium of straight and convoluted tubules. In one animal these bodies were found in large numbers in otherwise still normal organs. The affected animals had been fed cow serum in place of colostrum.

AUTHOR'S SUMMARY.

DOUBLE VITAL STAINING WITH BRILLIANT VITAL RED AND NIAGARA SKY BLUE. F. B. DAVIES, R. C. WADSWORTH and H. P. SMITH, J. Exper. Med. **51**:549, 1930.

Vital staining reactions of brilliant vital red and Niagara sky blue are studied in dogs and in rabbits. Either dye alone is taken up to form red or blue granules within the cytoplasm of macrophages and of certain other cell types. When the two dyes are injected simultaneously into the blood stream one finds that these cells build up granules which are purple from admixture of the two dyes. When several daily injections of one dye are followed by several daily injections of the other, one finds blue granules and red granules side by side within the cells, but no purple granules are found. This is thought to indicate that the dye is deposited in small foci which are active in a rather transitory way, and that the color of the granule is determined during its formative stage by the type of dye present in the fluids about the cell. The enlargement of phagocytic cells and the increase in their number with large dosage, or with repeated offerings of the dye, represent a method by which the cells maintain their phagocytic powers at the normal level. Evidence is offered to indicate that these and perhaps other compensatory changes may take place with great rapidity, so that it has been impossible to "block" or even reduce noticeably the ability of these cells to take up additional quantities of dye. Certain pitfalls in the experimental study of "blockade" are pointed out.

AUTHORS' SUMMARY.

THE EFFECT ON THE RATE OF UREA EXCRETION OF CARMINE DEPOSITION IN THE CELLS OF THE RENAL TUBULES. EATON M. MACKAY and LOIS LOCKARD MACKAY, J. Exper. Med. **51**:609, 1930.

The evidence that urea is present in high concentration in the cells of the convoluted tubules of the kidney and is passing through these cells has been reviewed. Following the deposition of a large amount of carmine in the cells of the convoluted tubules the rate of urea excretion, as measured by the relation of the rate of urea excretion to the blood urea concentration, is increased. This is interpreted as due to blockade or damage to the cells of the convoluted tubules which interferes with their usual function of absorption of urea and other sub-

stances from the glomerular filtrate and hence increases the amount of urea which reaches the bladder urine at a given blood urea concentration.

AUTHORS' SUMMARY.

ABNORMALITIES PRODUCED IN THE CENTRAL NERVOUS SYSTEM BY ELECTRICAL INJURIES. ORTHELLO R. LANGWORTHY, J. Exper. Med. **51**:943, 1930.

The alternating and continuous circuits produced different types of lesions in the central nervous system. Hemorrhages were common after alternating current shocks and few hemorrhages were observed in the continuous circuit group. With both types of circuits at 1,000 and 500 volts potential, severe abnormalities in the nerve cells were observed. These were more marked in the continuous circuit group. A uniformly staining, shrunken, pyknotic nucleus was taken as a criterion of nerve cell death. The Purkinje cells of the cerebellum were most susceptible to the current. Injured cells were studied in the dorsal nucleus of the vagus, in the somatic motor group, among the primary sensory neurons and in the olives. Changes in the histologic structure of the cells in reference to recovery have been discussed. Injury to the cerebral and cerebellar cortices occurred on the dorsal surface close to the head electrode. Small cavities were produced, particularly in the cerebral cortex, as the result of the circuit contract. With the continuous and alternating circuits at 110 and 220 volts potential, less severe changes were observed in the nerve cells although hemorrhages were common in the alternating circuit group. It must be assumed in these cases that death was due to respiratory block rather than to actual death of the cells.

AUTHOR'S SUMMARY.

BLOOD CYTOLOGY OF THE RABBIT. LOUISE PEARCE and ALBERT E. CASEY, J. Exper. Med. **52**:145 and 167, 1930.

The periods of greatest irregularity in mean neutrophil and eosinophil values occurred in the fall and the late winter and spring months of both years during which observations were made, but in the case of the basophils, the irregularities were distributed throughout the first year and occurred chiefly in the winter months of the second year. The major trends, and many of the minor fluctuations, as well, which were observed in the mean cell values of one group of rabbits were also generally seen in another group examined during the same months. The general levels of the neutrophil, basophil, and eosinophil mean values were higher in the groups examined during 1927 and 1928 than in the examined groups during 1928 and 1929. The general levels of the lymphocyte and monocyte mean values were higher in the groups examined during 1927 and 1928 than in the groups examined during 1928 and 1929. The results based on the trends of mean group values, obtained from consecutive weekly observations, showed no evidence of a consistent numerical relationship between lymphocytes and monocytes.

AUTHORS' SUMMARY.

EXPERIMENTAL NEPHRITIS IN THE FROG. JEAN OLIVER and PEARL SMITH, J. Exper. Med. **52**:181, 1930.

The damage produced by corrosive mercuric chloride, U. S. P., potassium bichromate and uranium nitrate in the frog's kidney is described. The morphologic lesions consist of tubular damage, such as regressive changes in the epithelium, and of damage to the glomeruli, ranging from increase in their permeability to gross damage of, and hemorrhage from, the tuft. The point is emphasized that these lesions differ in their degree, rather than in their nature, from those found in the mammalian kidney after the administration of the same poisons. The frog's kidney is exceptionally well suited, therefore, for the study of lesions which, though present, are masked in the complexities of structure and function of the mammalian kidney.

AUTHORS' SUMMARY.

THE ORIGIN AND FATE OF TWO TYPES OF MULTINUCLEATED GIANT CELLS IN THE CIRCULATING BLOOD. CLAUDE E. FORKNER, J. Exper. Med. **52**:279, 1930.

It has been demonstrated that giant cells of the foreign body and epithelioid types can be induced to appear in the blood stream. Evidence has been presented which indicates that foreign body giant cells are primarily formed by fusion of monocytes, and that the fate of these giant cells is accomplished, at least in some instances, by a separation into the constituent elements. Further evidence has been presented which lends support to the hypothesis that "epithelioid giant cells" reach their stage of evolution, not by fusion of monocytes, but by amitotic division of the nuclei of monocytes and epithelioid cells. The presence of giant cells in the peripheral blood as the result of injections of agar is almost invariably associated with, or preceded by, a marked monocytosis in which the new monocytes are of large size and show evidence of immaturity. Injections of agar into the tissues result in decreased absolute and percentage values of lymphocytes and a diminution of the specific granules in many of the polymorphonuclear leukocytes. It would appear from these studies that a clear differentiation of "epithelioid giant cells" and "foreign body giant cells" in the blood is usually possible, but that, on the other hand, a few cells may be present which have some of the characteristics of each type. The latter probably represent in their formation both a fusion of individual cells and an amitotic division of the nuclei of monocytes. Clasmatocytes or macrophages have in rare instances been seen to take part in the formation of foreign body giant cells. At least one instance has been noted of the fusion of a clasmatocyte with several monocytes. No evidence is available to demonstrate that macrophages ever play a part in the formation of "epithelioid giant cells."

AUTHOR'S SUMMARY.

GENETIC RELATIONS OF MONOCYTES. CLAUDE E. FORKNER, J. Exper. Med. **52**:385, 1930.

The theories for the origin of monocytes from myeloblasts, lymphocytes, endothelium, macrophages and primitive cells are reviewed and considered. Monocytes in all stages of development have been demonstrated to be present constantly in large numbers in all the lymph nodes of the body, except in the large mesenteric group. The relations of these cells to undifferentiated cells, lymphocytes, macrophages, plasma cells and endothelium are described. The origin of adult monocytes from primitive undifferentiated cells through the stages of monoblasts and premonocytes is described and illustrated. The demonstration in certain lymph nodes of innumerable monocytes in all stages of development permits a shifting of the term "monoblast" from the position of a more or less theoretical name to its proper place as a term designating that particular cell which is derived from a primitive undifferentiated cell and which is the immediate precursor of the premonocyte. The term "premonocyte" is proposed to designate the intermediate stage between the monoblast and the mature monocyte. Evidence is advanced to show that monocytes are an independent strain of cells, but that under physiologic conditions they may be transformed into macrophages, this representing at least one way in which the latter are normally produced. In no organs or tissues other than in certain specific lymph nodes, chiefly the peripheral group, can one constantly find monocytes in all stages of development. Developing monocytes occasionally may be found in small numbers in the spleen, mesenteric lymph nodes, Peyer's patches, subcutaneous connective tissues, lungs and omenta of normal rabbits, but their presence is by no means constant and their numbers are insignificant in comparison with those found in the peripheral lymph nodes. Monocytes and premonocytes do not stain by the common methods used for the demonstration of the reticulo-endothelial system and therefore must be considered for the present as independent of this system, except so far as monocytes may be transformed into macrophages. Plasma cells, stained with the supravital technic, as seen in

lymph nodes, are described. No basis has been found for the theory that plasma cells and monocytes are closely related structural elements.

AUTHOR'S SUMMARY.

AN ANATOMICAL STUDY OF SUBDURAL HEMORRHAGE ASSOCIATED WITH TENTORIAL SPLITTING IN THE NEWBORN. W. H. CHASE, Surg. Gynec. Obst. **51**:31, 1930.

This communication contributes an etiologic and anatomic analysis of a series of thirty-two cases of subdural hemorrhage associated with tentorial splitting in the new-born infant. The blood is largely supratentorial and often bilateral as a result of stretching or rupturing of the small tributaries of the great cerebral vein near its junction with the straight sinus. The most important predisposing factor to intracranial hemorrhage and tentorial splitting is prematurity, in that the dural septal fibers are of greater immaturity. The method of examination, the anatomy and the clinical aspects are adequately discussed.

RICHARD A. LIFVENDAHL.

LIPIODOL PELVIC CYSTS. A. F. LASH, Surg. Gynec. Obst. **51**:55, 1930.

Few instances of nonabsorption or untoward effects of iodized poppy seed oil 40 per cent have been reported, although this opaque medium has been used in the spinal and cerebral spaces, genito-urinary organs and pericardial, pulmonary, joint and peritoneal cavities. The presence of an infection of the female generative tract is regarded as a contraindication to the use of this diagnostic medium, for the oil has not been demonstrated to have antiseptic properties; a foreign body reaction may be induced in the pelvis. In the author's case, this occurred after injection of the oil into a uterus bicornis unicollis associated with chronic salpingitis, although the function of the tubes was not disturbed by the iodized oil, as the patient delivered a full term child one year after the injection. Laparotomy, twenty-two months after the diagnostic injection, revealed pelvic adhesions in which were cysts filled with clear, light amber, oily fluid, and surrounded each by a connective tissue capsule lined by histiocytes and foreign body giant cells outside of this capsule.

RICHARD A. LIFVENDAHL.

URETHRAL CARUNCLE IN THE FEMALE. C. T. OLCOTT, Surg. Gynec. Obst. **51**:61, 1930.

These dusky red pedunculated or broad-based growths of the lower half of the external urethral orifice are frequently regarded as malignant because of the marked infolding of the epithelium. In seventeen of twenty-three cases, a definite glandular mass was present in the submucosa, and to the author represented glands of Skene and therefore an important factor in the formation of caruncles.

RICHARD A. LIFVENDAHL.

GELATINOUS DEGENERATION OF THE BONE MARROW. PAUL MICHAEL, J. Path. & Bact. **33**:533, 1930.

Eleven cases of "gelatinous degeneration" of the bone-marrow were seen in 480 autopsies. In 4 of the 11 cases, tuberculosis was the cause of death; in 3, carcinoma; in 1 each, pyemia, degenerative productive nephritis, lymphogranulomatosis and ulcerative colitis. The average age was 40.1 years. The average duration of disease was 15.7 months. The proportion of males to females was 10:1. Gelatinous degeneration differs from uncomplicated edema of the bone-marrow in the presence of precipitated fibrin about the periphery of the fat cells. It is apparently the result of a reaction of fat and edema in the presence of fibrinogen, and should be considered as a lesion *sui generis* of the bone-marrow—best expressed as "hydrops fibrinosus of the bone-marrow." The latter expression should replace the indefinite term "gelatinous degeneration."

AUTHOR'S SUMMARY.

ENDOMETRIAL AUTOTRANSPLANTS IN THE RABBIT. H. H. GLEAVE, J. Path. & Bact. **33**:675, 1930.

The histologic appearance of autotransplants of endometrial tissue in the rabbit corresponds to that of the uterus of the same animal. Under the influence of the corpus luteum hormone (estrin) or after oophorectomy they show the same changes as the uterus.

AUTHOR'S SUMMARY.

VITAMIN D SCLEROSIS IN THE RAT'S AORTA. J. B. DUGUID, J. Path. & Bact. **33**:697, 1930.

The essential lesion of vitamin D sclerosis is a degeneration of muscle and calcification of the media similar to that seen in experimental adrenalin lesions in rabbits and in Mönckeberg sclerosis of the peripheral arteries in man. A secondary overgrowth of the intima from proliferation of intimal cells arises only when the adjacent subintimal layers are degenerate. It is a reparatory measure, and occurs when gross mechanical destruction is caused by masses of calcareous material in the subintimal layers being uprooted and thrust into the intima by the movements of the wall of the vessel. Fatty changes are secondary, and similar to the fatty changes seen in human atheroma. They occur most frequently in the subintimal layers of the media, and are associated with mechanical disturbances, such as shearing and stressing of the tissues between one layer and another.

AUTHOR'S SUMMARY.

ATROPHY OF THE ADRENALS ASSOCIATED WITH ADDISON'S DISEASE. WILLIAM SUSMAN, J. Path. & Bact. **33**:749, 1930.

Five cases of Addison's disease are recorded, in which the lesion in the suprarenal glands was a simple or fibroid atrophy, and it is found that about one fifth of all cases of Addison's disease are associated with this form of lesion. Atrophy of the suprarenal glands as a cause of Addison's disease appears to be more common in England than elsewhere. In cases of atrophy, both cortex and medulla are usually affected, but a lesion of the cortex is the more constant and in some cases may be the sole feature.

ADRENAL ATROPHY AND ADRENAL TUBERCULOSIS IN RELATION TO ADDISON'S DISEASE. F. F. HELLIER, J. Path. & Bact. **33**:761, 1930.

In 12,000 consecutive necropsies, 12 cases of Addison's disease occurred, in 6 of which there was tuberculosis, and in 3 atrophy, of the suprarenal glands.

ADRENAL ATROPHY IN ADDISON'S DISEASE. W. G. BARNARD, J. Path. & Bact. **33**:765, 1930.

In twenty-three cases of Addison's disease examined post mortem, the suprarenal glands were tuberculous in sixteen and atrophied in seven.

FIBRIL FORMATION OF EPITHELIOID CELLS IN TUBERCULOUS TISSUE. I. WALLGREN, Arb. a. d. path. Inst. zu Helsingfors **6**:51, 1930.

In tubercles, as well as in tuberculous granulation tissue, there is a rich formation of fibrils which do not stain by the usual methods, but which appear after impregnation with silver nitrate. The fibrils lie in the ectoplasm of the cells and resemble those of the fetal mesenchyme. There are apparently two types of epithelioid cells. Those originating from reticulo-endothelium are capable of forming fibrils; those originating from lymphoid cells are not. As these fibrils mature, they sometimes stain with fuchsin and also seem to undergo hyaline degeneration. These fibrils are not fibrin. Their formation may influence healing in certain tuberculous lesions.

GEORGE RUKSTINAT.

AN ABERRANT ADENOMA OF THE THYROID GLAND. P. E. A. NYLANDER, Arb. a. d. path. Inst. zu Helsingfors **6**:235, 1930.

Nylander found a "struma, nodosa colloides, macrofolliculars papillaris," in an aberrant portion of thyroid gland. The tumor started to develop several months after thyroidectomy in a man.

GEORGE RUKSTINAT.

EXPERIMENTAL ACUTE DIFFUSE GLOMERULONEPHRITIS. R. HÜCKEL, Beitr. z. path. Anat. u. z. allg. Path. **84**:571, 1930.

In agreement with Vollhard, Fahr, Lichtwitz and others, the author recognizes two forms of glomerulonephritis, the localized and the diffuse. In the former a single capillary loop of the glomerulus is involved, or at most the capillaries of a lobule are involved, whereas in the diffuse form the entire capillary tuft takes part in the process. In the early stages of the latter, as seen in the human kidney, the glomerulus is increased in size, and the entire capillary tuft is swollen and exhibits an increased nuclear content, due in part to leukocytes within the capillary lumen and in part to endothelial proliferation. The capillaries contain little or no blood. Fahr has held inflammation of the tuft to be the primary and essential process in diffuse glomerulonephritis, whereas Vollhard and others have considered spasm of the afferent arteriole primary, to which the involvement of the tuft is secondary. Localized glomerulonephritis, which may be embolic and nonpurulent, bacterial as the result of the excretion of bacteria by the glomerulus, or toxic, may be produced experimentally. The author claims that the diffuse form has not been successfully reproduced experimentally. Experimental reproduction of the lesion is desirable because it would permit study of the early stages of the process, concerning which there is considerable dispute. Hückel used scarlet fever streptococcus toxin (Dick toxin), injecting it directly into the exposed renal vein, the injection being directed toward the kidney. At this point it may be noted that, as far as one may determine from the article itself, in his series of experiments he used only six rabbits, one of which served as a control for the injection into the renal vein of physiologic solution of sodium chloride in an amount equal to that used in the experiments with toxin. Two animals received 3.5 cc. of 1:100 toxin and 3 cc. of 2:100 toxin, respectively, and died after thirty-seven and nine and one half hours. Another animal received 1 cc. of undiluted toxin and was killed after sixteen hours. In the remaining two experiments, several days were allowed to elapse after a single or repeated injections in order to study the later stages of the process. The changes noted were increase in the volume of the capillary loops of the tufts, increased intracapillary cellularity due to what the author terms intracapillary exudation, slight proliferation of the endothelium and hyperemia. These changes, which are characteristic for human diffuse glomerulonephritis, in the absence of detectable alterations in the afferent vessels, the author considers proof that the process is primarily an inflammation of the capillary tuft. Although in the experiments of longer duration there were noted changes comparable with the later stages of human glomerulonephritis, the most striking reaction was a diffuse interstitial subacute inflammatory process.

O. T. SCHULTZ.

ACUTE PEPTIC DUODENITIS. H. RADECKE, Beitr. z. path. Anat. u. z. allg. Path. **84**:617, 1930.

As a contribution to the contention of the Aschoff school that the gastric juice may exercise a caustic action and may cause localized erosions and ulcerations from which the typical peptic ulcer of the stomach may develop, Radecke presents a study of lesions encountered post mortem in the duodenum in three cases. The lesions were most numerous in the upper part of the duodenum and were absent at and below the level of the papilla of Vater. They were localized and not diffuse and were situated on the crests of the rugae of the mucosa of the anterior and posterior walls of the duodenum. The earliest and smallest lesions were micro-

scopic. In these the epithelium of the tips of the villi had undergone hyaline fibrinoid necrosis, and a few leukocytes were present in the tissue about the necrotic epithelium. In larger and presumably slightly older lesions, the necrotic material had been thrown off, resulting in erosions and superficial ulcerations, with leukocytes and fibrin at their base. The lesions are believed to have been of relatively few hours' duration. They were identical with those that Büchner and others of Aschoff's institute have described in the stomach as due to the action of gastric juice. Their location and local character are ascribed to the course of the fluid in the duodenum after the gastric juice leaves the stomach.

O. T. SCHULTZ.

EXPERIMENTAL GASTRITIS DUE TO DILUTE HYDROCHLORIC ACID. E. GOTSCHLICH, Beitr. z. path. Anat. u. z. allg. Path. **84**:632, 1930.

In order to reproduce the acute lesions of the human stomach that Aschoff and his pupils have ascribed to the caustic action of the gastric juice, Gotschlich introduced by stomach tube from 15 to 20 cc. of from 0.8 to 1.5 per cent of hydrochloric acid into the empty stomachs of cats. In acute experiments, in which the animals were killed after from six to twelve hours, no food was given after the administration of the acid. In experiments of longer duration food was permitted from eight to ten hours after the administration of the acid. The pyloric portion of the stomach of cats that had received acid was found to be firmly contracted when the animals were killed, and the mucosa of this portion of the stomach was free from lesions. The lesions were situated in the mucosa proximal to the pyloric region. They were multiple, and were circumscribed and localized rather than diffuse. They were limited to the crests of the rugae of the mucosa. The smallest and earliest lesions were microscopic in size and presented the change described by the Aschoff school as characteristic of the local caustic action of gastric juice. The epithelium at the tips of the villi was necrotic and glassy, and stained deeply with eosin. The necroses were sometimes of a hemorrhagic character, a fact which is submitted as evidence to controvert the statement that the presence of hemorrhage is proof of the vascular origin of gastric erosions. In lesions of slightly longer duration, the necrotic material was cast off. The floors and sides of the erosions and superficial ulcers thus formed were infiltrated by leukocytes and contained fibrin. The inflammatory reaction is secondary to the caustic action of the acid. Evidences of repair of the lesions were noted early, within from eight to thirty-six hours after administration of the acid. The changes noted in the healing lesions were identical with those that Konjetzky and Puhl have described in the surgically resected human stomach as the lesions of an exogenous gastritis which they hold responsible for gastric ulcer. The healing lesions are not specific. The acute lesions are specific and characteristic of the action of the acid of the gastric juice. This initial stage was not seen by Konjetzky and Puhl in their material because it is of short duration and is transformed into the healing lesion by the preoperative treatment to which patients are subjected.

O. T. SCHULTZ.

A SPONTANEOUS PARARENAL HEMATOMA IN ACUTE MYELOID LEUKEMIA. A. GAÁL, Centralbl. f. allg. Path. u. path. Anat. **49**:33, 1930.

A huge right pararenal hematoma was found in the body of a 47 year old man dying from myeloid leukemia. It was apparently of extrarenal origin, extended through the fatty capsule, and was in contact with collections of blood in muscles altered by myeloid infiltrations. Such hematomas occur only once in the course of disease of the kidney as against eleven times from extrarenal sources. The extrarenal causes are trauma, hemophilia and hemorrhage in the course of sepsis or of such diseases as scarlet fever or leukemia.

GEORGE RUKSTINAT.

ATHEROSCLEROSIS IN PARROTS. M. HESSE and K. WALKOFF, Centralbl. f. allg. Path. u. path. Anat. **49**:40, 1930.

The arteries of two parrots, one 48 years old and the other 60 years old, were altered by fatty and hyaline regions as in typical atherosclerosis seen in senile human beings or in guinea-pigs fed diets rich in fat. Age seems to be a factor in bringing about these changes in parrots, although similar changes are not seen in birds kept on natural diets in zoological gardens.

GEORGE RUKSTINAT.

TWO UNUSUAL CYSTS OF THE THYROGLOSSAL DUCT. R. BAYER, Centralbl. f. allg. Path. u. path. Anat. **49**:137, 1930.

The two cysts described occurred in an unusual position, namely, below the hyoid bone. Most of these cysts are found near the base of the tongue. The difference in age between the persons from whose bodies the cysts were obtained was also noteworthy; one cyst was found in an 8 weeks old boy, and one in a 78 year old woman.

GEORGE RUKSTINAT.

A SPONTANEOUSLY HEALED DISSECTING ANEURYSM OF THE AORTA. M. PLONSKIER, Centralbl. f. allg. Path. u. path. Anat. **49**:161, 1930.

In the body of a woman, 55 years old, who had suffered from cardiac weakness for several years, a dissecting aneurysm extended from 3 cm. distal to the right renal artery to the bifurcation of the left common iliac artery. It involved the aortic wall in front for 8 by 4.5 by 4 cm. and the iliac artery for 8 by 3 by 2 cm. The lining of the wall of the aneurysm was smooth and resembled intima. The original proximal opening into the aneurysmal space was healed, but there was still a minute opening distally into the lumen of the left common iliac artery.

GEORGE RUKSTINAT.

SYPHILIS OF THE PULMONARY ARTERY. T. REEKE, Centralbl. f. allg. Path. u. path. Anat. **49**:257, 1930.

In the body of a woman, 50 years old, dying of cardiac decompensation, a syphilitic aneurysm of the right ventricle and syphilitic mesarteritis of both the pulmonary artery and the aorta was found. There was a widening of the commissure between the pulmonic leaflets. In 1928, the Wassermann reaction of the blood was $+++$ and in 1929, $++$, and blood removed from the body post mortem gave a negative reaction, whereas pericardial fluid gave a positive reaction.

GEORGE RUKSTINAT.

THE NUMBER OF BASOPHIL CELLS IN THE HUMAN HYPOPHYSIS IN AMYLOIDOSIS OF THE KIDNEYS AND SUPRARENAL GLANDS. H. LITTNA, Frankfurt. Ztschr. f. Path. **40**:124, 1930.

Contrary to the observations of others, the author reports that the basophil cells in the anterior lobe of the hypophysis in eighteen cases of amyloidosis of the kidneys have neither decreased nor increased in number. Because the majority of the suprarenal glands in these eighteen cases also showed amyloid, the question is raised whether the amyloidosis of the suprarenal glands alone may lead to an increase in the number of the basophil cells in the hypophysis, and amyloidosis of the kidneys alone to a decrease in the number of the cells. If so, amyloidosis of both organs would yield about the normal number of basophil cells. No relation could be demonstrated between the basophil content of the anterior lobe of the hypophysis and amyloidosis of other organs.

O. SAPHIR.

PRIMARY LYMPHOGRANULOMA (HODGKIN'S DISEASE) OF THE INTESTINES. P. HEILMANN, Frankfurt. Ztschr. f. Path. **40**:151, 1930.

The tumor described in this paper was removed from a woman 50 years old. The tumor was located in the cecum in the region of the mesenteric attachment,

and measured 3 by 6 by 8 cm. On section the tumor was grayish white, presented a moist surface and was easily movable. In the mucosa of the colon close to this tumor, a round ulcer was noted, which measured 3 by 3.2 cm. Surrounding the tumor, the muscular coat of the intestine was distinctly hypertrophic. In the ileocecal region, enlarged lymph nodes were present, which were of firm consistency and which showed, on section, yellowish-white, well demarcated areas of necrosis. Microscopically, the lymph nodes contained many fibroblasts, endothelial cells, large and small round cells, eosinophil leukocytes and many Dorothy Reed cells. No bacteria could be demonstrated in the sections.

O. SAPHIR.

THE SIGNIFICANCE OF THE ARGENTAFFINE CELLS. G. ERÖS, Frankfurt. Ztschr. f. Path. **40**:155, 1930.

The author studies the influence of insulin, epinephrine, extirpation of the pancreas and thyroid gland and partial removal of the suprarenal glands on the number of argentaffine cells of the intestines. After injection of 10 units of insulin per kilogram of body weight into dogs over a period of one week (chronic insulin effect), the argentaffine cells increased markedly in number. The dogs were fed with a mixed diet. One dog was treated by injection of 30 mg. of epinephrine over a period of eight hours. The argentaffine cells were increased in number. To another dog, 30 mg. of epinephrine was given over a period of one week. The argentaffine cells showed a decrease in number. The pancreas of a cat fed with a mixed diet, was extirpated. Four days after operation, the cat was killed. The argentaffine cells were found to have increased in number. In a number of dogs and rabbits the suprarenal glands were cauterized. When the animals were kept alive longer than seven days, the argentaffine cells were found to be much more numerous than in normal animals. In one rabbit the thyroid gland was removed. The rabbit survived the operation thirty days. The argentaffine cells were more numerous than was normal. In starved animals the argentaffine cells at first seemed to have increased in number, but later disappeared. A rabbit that was kept at a temperature of 2 C. showed more argentaffine cells in the intestinal mucosa than a normal rabbit. The author concludes that in animals in which the blood sugar content has been lowered, the argentaffine cells at first decrease, but later increase, in number. In animals in which the blood sugar content has been increased, the argentaffine cells at first increase, but later decrease, in number.

O. SAPHIR.

CHRONIC THROMBOSIS OF THE PULMONARY ARTERY AND ITS MAIN BRANCHES. L. DESCLIN, Frankfurt. Ztschr. f. Path. **40**:161, 1930.

The author describes two cases in which the main pulmonary artery, and six cases in which the main branches of the pulmonary artery, were partially or completely occluded by thrombi. The origin of these thrombi is traced back with great probability to a primary embolus and secondary thrombosis.

O. SAPHIR.

LYMPHOID LEUKEMIA WITHOUT INVOLVEMENT OF LYMPH NODES. R. RÖSSLE, Virchows Arch. f. path. Anat. **275**:310, 1930.

Rössle presents two cases of chronic lymphoid leukemia in which the usual and characteristic hyperplasia of the lymph nodes was absent. In the first patient, a man aged 85, the duration of the abnormal state of the blood was not known. The leukocyte count was 97,500, with 70 per cent lymphocytes. None of the lymph nodes was enlarged. On microscopic examination the nodes did not appear hyperplastic. The spleen weighed 220 Gm., and was completely transformed into tissue composed only of small lymphocytes. Pulp cells and sinusoids could not be recognized. Moderate lymphoid hyperplasia was present in the bone marrow. The second case receives fuller discussion because of its rarity. The patient, a woman, aged 61, had been under observation for many years, having been first

seen at the age of 35, for a lesion of the leg that had recurred each winter for the previous ten years. The lesion was at first considered mycosis fungoides or premycotic erythrodermia, but in the course of time the typical blood picture of lymphoid leukemia developed, and the condition of the skin was held to be leukemia cutis. Necropsy yielded no gross or microscopic evidence of lymphoid hyperplasia of the lymph nodes, spleen or bone marrow. Sections of the skin from various parts of the body revealed a layer of cellular lymphadenoid tissue beneath the epidermis. The tissue was composed of reticulo-endothelial cells and small lymphocytes, supported by a reticulum like that of lymphoid tissue. Rössle believes that the lymphocytes of the skin and circulating blood arose locally in the skin from reticulo-endothelial cells, and that the transformation occurred without an intervening lymphoblast stage. He considers the case a unique one of leukemia or lymphadenia cutis, because the lymphoid hyperplasia was limited to the skin. In neither of the cases described was there leukemic infiltration of the internal organs.

O. T. SCHULTZ.

FETAL ERYTHROLEUKOBLASTOSIS. E. VON GIERKE, Virchows Arch. f. path. Anat. **275**:330, 1930.

The basis of von Gierke's report is a female child, born at full term, that died one hour after birth. Seven years previously he had examined postmortem a female child of the same parents, that died fifty hours after birth. That child revealed marked erythroblastosis, without edema. The parents were healthy; it is especially noted that both were free from syphilis. The infant that is the subject of the present report died as the result of intraperitoneal hemorrhage from a ruptured spleen. The latter organ weighed 112 Gm. and extended beyond the midline of the abdomen and below the level of the umbilicus. Blood smears contained an abnormally large number of erythroblasts, chiefly normoblasts, and of leukoblasts, identified as myeloblasts and neutrophil and eosinophil myelocytes. The liver, spleen and kidneys contained numerous focal areas of erythroblastic and leukoblastic tissue. The liver cells were laden with hemosiderin and iron-free pigment. The blood contained the pigment xantorubin, previously detected only in hepatectomized dogs. Its presence is interpreted by von Gierke as evidence of severe damage to the liver. There was no edema. Fetal erythroblastosis is frequently associated with generalized anasarca of the fetus and with an abnormally large placenta. Fetal erythroblastosis has been held to be fetal anemia, to which the edema is secondary. Von Gierke points out that edema may be absent, as in his two cases, and that when present, it has usually been in stillborn or moribund infants. He considers the condition as it existed in the second child more closely related to leukemia than to anemia. Because of the lability and multiple potencies of the fetal hematopoietic system, the unknown stimulus to proliferation of leukoblastic tissue may also act on the erythroblastic tissue, sometimes to a greater degree than on the leukoblastic tissue. The condition is a systemic disease of the hematopoietic tissues. It is associated with a disturbance of hemoglobin metabolism, which manifests itself by jaundice and by the deposition of iron-free and iron-containing pigment in the tissues. In his first case there was marked "Kern" icterus of the basal ganglions of the brain.

O. T. SCHULTZ.

Pathologic Chemistry and Physics

SERUM-CALCIUM IN PNEUMONOCONIOSIS. MARTIN J. SOKOLOFF and A. CANTAROW, Am. Rev. Tuberc. **22**:449, 1930.

In a group of thirty patients with pneumonoconiosis, fifteen of whom had an associated active tuberculous lesion, the serum-calcium ranged from 7.98 to 14.81 mg. per one hundred cubic centimeters, being above normal in twenty-six patients, subnormal in one and normal in three. The serum-calcium level bore no relation to the incidence or activity of the complicating tuberculous process.

The hypercalcemia in pneumonoconiosis is in all likelihood dependent on the increase in the carbon-dioxide tension of the blood, which is an inevitable consequence of the pulmonary lesion.

H. J. CORPER.

THE INORGANIC PHOSPHORUS OF THE BLOOD IN RICKETS. A. F. HESS, MILDRED WEINSTOCK, H. RIVKIN and J. GROSS, J. Biol. Chem. **87**:37, 1930.

The decrease in the inorganic phosphorus of the blood, which is often associated with rickets, does not appear to be an essential or inherent feature in the pathogenesis or in the healing of the disease. If calcium or phosphorus in a favorable ratio, as in milk, are included in a rachitogenic diet, the addition of small amounts of viosterol to the diet may be followed by an increase in the inorganic phosphorus without healing of the rachitic lesions. The addition of larger amounts of viosterol is followed by prevention and healing. The addition of cod liver oil to the diet is followed by definite healing, although the phosphorus value attained is not high. A local disturbance at the epiphyses may prevent the anchorage of calcium and phosphorus in the cartilage of the bones.

E. R. MAIN.

LIPIDS IN XANTHOMA. H. C. ECKSTEIN and U. J. WILE, J. Biol. Chem. **87**:311, 1930.

Tumor fat appears to have a higher iodine value and to contain a larger proportion of the more highly unsaturated fatty acids than normal human subcutaneous fat or the fat adhering to tumors. The total lipids of the tumor fat contain 48.81 per cent of cholesterol and 8.1 per cent of phospholipid, concentrations that are 200 times in excess of those found in normal fat. The nature of the lipids in xanthomas appears to be more dependent on the activity of the tissue than on the nature of the lipids present in the blood.

E. R. MAIN.

A CRYSTALLINE DERIVATIVE OF AN ACID IN THE LIVER IN PERNICIOUS ANEMIA. RANDOLPH WEST and MARION HOWE, J. Biol. Chem. **88**:427, 1930.

A crystalline salt of an acid which is effective in producing the remission of pernicious anemia has been isolated from a highly purified preparation of liver extract. Analyses indicate that the acid may be β-hydroxy-glutamic acid.

E. R. MAIN.

THE COPPER CONTENT OF INFANT LIVERS. D. B. MORRISON and T. P. NASH, JR., J. Biol. Chem. **88**:479, 1930.

The average content of copper in the livers of infants is 24 mg. per kilogram of fresh tissue, about six times that of the livers of adults.

E. R. MAIN.

CHEMICAL ALTERATIONS IN THE BLOOD OF RATS INFECTED WITH TRYPANOSOMES. R. W. LINTON, J. Exper. Med. **52**:695, 1930.

Samples of blood from rats infected with *Trypanosoma lewisi* give normal values for lipoid phosphorus, lecithin, carbon dioxide—combining capacity, and liver glycogen. When these results are compared with the results of similar experiments with *T. equiperdum* infections, on the basis of concentration of trypanosomes in the blood, it is found that the pathogenicity of the latter organism does not depend on its numbers as affecting the blood, but that it must be in some other way injurious to the host. Whether the injury is due to a true toxin, an endotoxin, or mechanical interference is not yet known.

AUTHOR'S SUMMARY.

COPPER CONTENT OF HUMAN ORGANS. H. KLEINMANN and J. KLINKE, Virchows Arch. f. path. Anat. **275**:422, 1930.

The rôle ascribed by Mallory to chronic intoxication by copper in the etiology of hemochromatosis has led to the development of new methods for the quantitative estimation of minute amounts of copper in the tissues. The authors modified slightly the colorimetric method of Schönheimer and Oshima. They give in detail the technical procedure used by themselves. The average error of the method in control blank analyses was 1.7 per cent, and in control analyses of tissues to which known amounts of copper had been added the error was 3.6 to 6.8 per cent. Their results are tabulated as milligrams of copper per kilogram of dried substance in the case of organs examined and as milligrams of copper per liter in the case of blood. The copper content of twelve normal adult livers varied from 11.8 to 48.7 mg., with an average of 27.5 mg. These figures are slightly higher than those of Schönheimer and Oshima. Two samples of blood contained, respectively, 1.7 and 1.4 mg. of copper. A sample of cardiac muscle contained 2.2 mg., and one of skeletal muscle, but from another and younger person, contained 1.8 mg. of copper. The copper content of the liver in a typical case of hemochromatosis was 133 mg., a decided increase above the normal average. The liver in another case considered hemochromatosis, but with the pigmentary changes limited chiefly to the intestine, contained 18.3 mg. of copper. Two livers with nonpigmented cirrhosis contained, respectively, 8.7 and 3.9 mg. of copper. Of greatest interest are the relatively large amounts of copper found in the livers of fetuses and new-born infants. The copper content of ten such livers varied from 137.5 to 450 mg., with an average of 303 mg. The copper content of livers of three children, aged, respectively, 13 weeks, 14 months and 2 years, varied from 12 to 26 mg. The thoroughly transfused liver of a new-born infant contained 516 mg. of copper, proving that the high copper content of the liver at this period of life is not due to the copper of the blood in the organ. The large amount of copper in the liver of the fetus and of the new-born infant is interpreted as evidence of the important functional rôle of this element in the normal physiology of the fetus and of the very young infant.

O. T. SCHULTZ.

THE EFFECT OF PITUITARY ON THE IONIC OUTPUT IN THE URINE. T. POULSSON, Ztschr. f. d. ges. exper. Med. **72**:232, 1930.

Following intramuscular injections of pituitary, in doses of from 10 to 15 units, characteristic changes in the ionic content of the urine were noted. The amount of total fixed base in proportion to the amount of sodium was increased. There was a decrease in the ammonia fraction, although the actual reaction of the urine was more alkaline.

PEARL ZEEK.

BLOOD CHEMISTRY IN PUERPERAL INFECTION. E. O. GAESSLER, Ztschr. f. d. ges. exper. Med. **72**:726, 1930.

Successive determinations of the alkali reserve, blood sugar and lactic acid in the blood during the various stages of puerperal infection revealed characteristic values, which facilitate a differential diagnosis, besides being of value to prognosis and therapeusis.

PEARL ZEEK.

Microbiology and Parasitology

CHRONIC EPIDEMIC ENCEPHALITIS. W. B. STEWART and M. J. EVANS, Am. J. M. Sc. **180**:256, 1930.

The Pfeiffer bacillus was isolated from all the nasopharyngeal cultures from 165 patients with chronic encephalitis. The serums from these patients agglutinated the Hammett strain of this bacillus. Of the control series, 46 per cent of naso-

pharyngeal cultures were positive for the Pfeiffer bacillus, but of 122 nonencephalitic serums, 114 neither agglutinated nor flocculated this bacillus. Of 20 cases of chronic encephalitic Parkinsonism studied for sinus disease, 18 gave positive results either by roentgen or clinical examination; 13 of these had definite disease of the ethmoids. Of 46 patients with chronic encephalitic Parkinson's disease treated for one month or more with the soluble antigen, 78 per cent showed improvement. This was not considered as due to a nonspecific protein reaction, because the amount of protein involved was so small.

JOHN PHAIR.

TISSUE REACTIONS IN RABBITS FOLLOWING INTRAVENOUS INJECTION OF BACTERIA. R. N. NYE and F. PARKER, JR., Am. J. Path. **6**:381, 1930.

Following the intravenous injection into rabbits of relatively large doses of various dead bacteria, there is a marked reaction of the tissues that contain cells of the reticulo-endothelial system. This reaction consists in an increase of lymphoid cells, which are eventually transformed into, or replaced by, monocytes and giant cells. Such lesions ordinarily are temporary and result in no permanent damage. Identical lesions occur after the intravenous injection into rabbits of various colloidal substances. Such changes represent the reaction of normal rabbits in the disposition of foreign materials in the blood stream and have nothing to do with reactions secondary to sensitization or immunization.

AUTHORS' SUMMARY.

A BACTERIOLOGICAL AND CLINICAL STUDY OF GASTRIC ULCER. E. WATTS SAUNDERS, Ann. Surg. **92**:222, 1930.

On the basis of bacteriologic work, the infectious theory of gastric ulcer is supported, rather than the vascular, toxic, neurologic or chemical explanations, because of the following observations: A streptococcus was isolated from nineteen resected gastric or duodenal ulcers. This organism proved to be identical and specific by differential culture tests, agglutination, cross-agglutination and agglutinin absorption. Its agglutinogenic and antigenic identity with similar strains producing ulcers of mucous membranes and skin was demonstrated, and likewise its non-identity with strains from foci of infection, appendicitis and cholecystitis was shown. In 100 per cent of the cases tested there were specific agglutinins in the blood serum, whereas these did not occur in other types of streptococcus infections. It is suggested that the marked formation of lactic acid by this organism may have some relation to carcinomatous degeneration.

RICHARD A. LIFVENDAHL.

TRACHOMA AND AVITAMINOSIS. A. I. KENDALL and S. R. GIFFORD, Arch. Ophth. **4**:322, 1930.

The authors report experiments designed to test the effects of vitamin A deficiency per se as a predisposing factor to infection with *Bacillus granulosis*. White rats were used and cultures of *Bact. granulosis*. Fresh trachomatous material was inoculated. Three series of rats were tested as follows: rats deprived of vitamin A for thirty days and exhibiting keratomalacia before inoculation; rats deprived of vitamin A for ten days before inoculation, and rats deprived of vitamin A for ten days, then inoculated, first with cultures of *Bact. granulosis* previously grown on rat-blood agar, and finally with cultures grown on Noguchi's leptospiral medium. Series 2 and 3 were kept on a vitamin-A-free diet for an additional eighteen days. No changes were seen in the eyes of the animals, even when inoculations of *Bact. granulosis* were preceded by injections of *Bacillus pseudotuberculosis-rodentium*, streptococci, etc., which caused a transitory inflammation.

"It must be admitted that the white rat may have a degree of resistance to the trachoma virus that transcends even the effects of a prolonged starvation of vitamin A."

Negative results attended the instillation of fresh trachoma material (from which *Bact. granulosis* was isolated) into the eyes of white rats thoroughly deprived of vitamin A. "In the light of the statements that dogs, cats and monkeys may spontaneously contract folliculosis, it would appear that the lack of success in inducing even a transitory reaction with fresh trachoma material after deprivation of vitamin A is suggestive that such deprivation per se is not necessarily a factor in trachoma infection. This, however, is not to be construed as an argument against the statement that deprivation of vitamin A is a contributory cause."

CHARLES WEISS.

EXPERIMENTAL SYPHILIS. G. C. LAKE and K. K. BRYANT, Bull. Nat. Inst. Health, 157, 1930.

The lymph gland transfer method for the determination of the presence of the *Treponema pallidum* in human cases of syphilis was applied in sixty-six instances. The group included thirty-four early cases in untreated patients, fifteen early cases in partially treated patients, nine old cases (average duration 6.9 years; in insufficiently treated patients, and eight old cases (average duration 22.5 years) in untreated patients. We were able to demonstrate the spirochete in the testicles of rabbits inoculated with emulsified lymph glands from each of the thirty-four untreated patients with early syphilis and from four of the nine insufficiently treated patients with old syphilis. All of the other transfers yielded negative results, even after subculture to a second group of animals. The results obtained indicate the impracticability of using the intratesticular injection of emulsions of human lymph glands into rabbits as a method for determining the presence or absence of syphilis in man, except in the early stages in untreated patients. Similarly our work shows the impracticability of applying this method to the measurement of the chemotherapeutic activity of the arsenicals in the treatmen of patients with syphilis.

Our experience has shown us the value of using the results of two sensitive serologic tests as presumptive evidence of syphilis in rabbits and as indicating the degree of probability of being able to demonstrate the spirochete by the dark field examination of testicular puncture material from rabbits inoculated by the technic that we have employed. It has also shown us the value of the dark field examination of emulsion of the entire testicle into which injection was made as the final test for the presence of *T. pallidum,* particularly in the case of an "asymptomatic" animal.

The results which we obtained in the production of syphilis in the rabbit indicate that if careful clinical examinations are frequently made of the original group of inoculated animals, if sensitive and dependable serologic tests are employed, and if final dark field examinations are made of an emulsion of the entire inoculated testicle from each rabbit, subsequent subculturing of the negative animals into a second group of rabbits will not significantly increase the number of positive observations. The additional time and expense involved outweigh the results to be expected.

AUTHORS' SUMMARY.

BRUCELLA IN STOOLS AND BILE. H. L. AMOSS and MARY A. POSTON, J. A. M. A. **95**:482, 1930.

Brucella has been isolated seventy-eight times from the stools of six patients. The use of liver agar as the basis for the eosin-methylene blue plates offers no improvement over the use of meat extract agar. *Brucella* has been obtained in cultures from the bile procured by duodenal drainage and from the contents of the gallbladder at operation in a case of chronic *Brucella* infection. The causative organisms may not always be present in the stools in acute cases of *Brucella* infection.

PSITTACOSIS. J. M. RIVERS, G. P. BERRY and C. R. RHOADS, J. A. M. A. **95**:579, 1930.

The virus of psittacosis is in the feces and in the material collected from the nose, mouth and procrop of infected parrots. Parrots and monkeys can be infected by intranasal instillations of the virus. Parrots and rabbits that have recovered from a primary infection are refractory to reinfection. It is not a simple matter to demonstrate neutralizing properties in convalescent human serum. In parrots and in mice, the principal lesions occur in the liver and spleen. Young monkeys (*Macacus rhesus*) are susceptible to intracerebral, intratracheal and intranasal inoculations of psittacosis virus. When it is instilled into the nose or injected into the trachea a characteristic pathologic picture occurs in the lungs which is similar to that observed in man.

AUTHORS' SUMMARY.

STREPTOCOCCAL INFECTIONS OF EPIPHYSES AND SHORT BONES. D. B. PHEMISTER, A. BRUNSCHWIG and L. DAY, J. A. M. A. **95**:995, 1930.

Bacteriologic studies were made of biopsy material in two cases each of Köhler's disease of the tarsal scaphoid, Legg-Perthes' disease and Kienboch's malacia of the os lunatum. Streptococci grew in cultures in four of the cases; cultures in two remained sterile. A streptococcus that on blood agar plates was more hemolyzing than green-producing and on dextrose blood agar plates more green-producing than hemolyzing grew in cultures in one case of Köhler's disease showing acute symptoms. Green-producing streptococci grew in cultures in one case of Legg-Perthes' disease and in one case of Kienboch's malacia. A streptococcus that was not further identified grew in cultures in one case of Kienboch's malacia. One case of Köhler's disease in which the cultures and the results of guinea-pig inoculations were negative occurred in association with multiple osseous and lymph-glandular tuberculosis. One apparent case of Köhler's disease developed following traumatism. These observations suggest that streptococci play an important rôle in the etiology of these diseases, but that other factors may also bring them about. Whether the streptococci reach the bone in an embolus which blocks the main artery or whether they lodge there alone remains undetermined.

AUTHORS' SUMMARY.

RELATIONSHIP OF THE SCROTAL SWELLING AND RICKETTSIA BODIES TO MEXICAN TYPHUS FEVER. M. RUIZ CASTANEDA, J. Exper. Med. **52**:195, 1930.

Scrotal swelling can appear in guinea-pigs directly inoculated from a human case of Mexican typhus fever. With certain strains of this disease, a number of generations of guinea-pigs may show absolutely no scrotal swelling, which, however, may reappear in subsequent animals, suggesting, though not absolutely proving, that the scrotal swelling is an integral part of the disease and is not due to an incidental accompanying organism. If the latter were true, one would expect the organisms that caused the scrotal swelling to disappear during the negative generations. A typhus fever sustained by a guinea-pig without scrotal swelling protects against the swelling on subsequent inoculation with a strain that produces this with considerable regularity. Passage through lice increases the capacity of a strain to produce the scrotal lesion, probably because of the considerable accumulation of rickettsia in the louse; but in the experiment noted, even with a strain that had been passed through lice, absence of swelling for two generations occurred, followed by recurrence of the swelling.

AUTHOR'S SUMMARY.

SUSCEPTIBILITY OF RABBITS TO INFECTION BY THE INHALATION OF TYPE II PNEUMOCOCCI. ERNEST G. STILLMAN, J. Exper. Med. **52**:215, 1930.

The susceptibility of rabbits to infection by inhalation of *Pneumococcus* varies in direct proportion to the virulence of the organism for rabbits. When rabbits are exposed to a pneumococcus spray, irrespective of the virulence of the organism, the bacteria readily penetrate into the lower part of the respiratory tract. When rabbits are exposed to a spray of the avirulent, degenerated "R" form of *Pneumococcus,* septicemia does not occur, and pneumococci are seldom recovered from the liver, kidney or spleen. When rabbits are exposed to a spray of slightly virulent *Pneumococcus* Type II (SAv), a nonfatal septicemia may occur, and pneumococci may be recovered from the liver, kidney and spleen. When rabbits are exposed to a spray of virulent Type II (Sv) pneumococci, septicemia may occur which in certain instances terminates fatally. Pneumococci may also be recovered from the liver, kidney and spleen.

AUTHOR'S SUMMARY.

SURVIVAL AND MULTIPLICATION OF THE VIRUS OF POLIOMYELITIS IN VITRO. P. H. LONG, P. K. OLITSKY and C. P. RHOADS, J. Exper. Med. **52**:361, 1930.

The study here reported concerns attempts at bacteriologic cultivations with fragments of brain or cord, or with Berkefeld V filtrates of the nervous tissues, from seven monkeys successfully inoculated with poliomyelitic virus. With these materials, 315 tubes were inoculated, of which 36 showed minute bodies resembling the globoid bodies described by Flexner and Noguchi. However, a study of subplants from these minute, morphologic particles did not convince us that we had in hand actual cultures of the globoid bodies, or indeed of any living microorganism. Nevertheless, when washed sediments from subplants of one of the strains, representing the seventh, eighth, ninth and tenth transfers, were inoculated into monkeys, the clinical signs and pathologic effects characteristic of experimental poliomyelitis were induced. The virulence of the "cultures" could not be ascribed to carrying over the origin material into these remote subplants since the seventh transfer represented a dilution of the original cultivated material to about 1.5×10^{-12}, and the tenth, to about 1.3×10^{-18}, if one assumes, as the transfer technic justifies, a thorough mixing of the contents of each tube. On the contrary, it appears as if the poliomyelitic virus had multiplied in vitro, and had increased as a consequence of being in a medium of a modified living tissue-cell culture. For in practically all specimens we observed many well preserved kidney tissue cells and leukocytes, the latter probably derived from human ascitic fluid, a component of the Smith-Noguchi medium. In this connection, it should be mentioned that the several lots of ascitic fluid used in the cultivation tests were recently obtained from patients and employed for from a week to a month after their collection. There remains for consideration the problem of the selective pathogenicity of the "cultures": only the material of those tubes of the ninth and tenth transfers which showed the "globoid bodies" proved pathogenic; those respective tubes of the same transfers which were free from the minute bodies, but apparently identical in all other respects, were avirulent. It may be that the virus was adsorbed to the particular bodies that we have found in the "cultures" and that resemble closely the globoid bodies of Flexner and Noguchi. Further elaboration of this study would be necessary, however, before such an inference could be regarded as a definite hypothesis.

AUTHORS' SUMMARY.

CULTIVATION OF VACCINE VIRUS. C. P. LI and T. M. RIVERS, J. Exper. Med. **52**:465, 1930.

A strain of neurovaccine virus was cultivated in a medium consisting of minced chick embryo suspended in Tyrode's solution. The virus on cultivation apparently lost none of its essential characteristics. The culture virus can be preserved and stored for long periods of time. Furthermore, the preserved virus can be used to initiate fresh cultures.

AUTHORS' SUMMARY.

HOST FACTORS IN THE PATHOGENESIS OF PNEUMOCOCCUS PNEUMONIA. EZRA A. SHARP and FRANCIS G. BLAKE, J. Exper. Med. **52**:501, 1930.

The present study was undertaken in order to determine whether animals exhibiting cutaneous hypersensitiveness to pneumococcus would show an acute inflammatory reaction in the lungs when pneumococcus autolysate was brought into contact with the pulmonary tissues, and, if so, whether the pulmonary reaction might be shown to be due to the allergic state of the animal, rather than to intrinsic properties of the autolysate. Twenty young rabbits were sensitized to pneumococcus by various procedures, and their degree of hypersensitiveness was determined at frequent intervals over varying periods of time by means of intracutaneous injections of pneumococcus autolysate standardized on the basis of nitrogen content and so treated as to be devoid of the known toxic principles. Twenty-four hours after the last skin test, each rabbit was given an intratracheal injection of the same pneumococcus autolysate. Seven nonsensitive controls were given similar injections intratracheally. Twenty-four hours after the intratracheal injection, the rabbits were killed. The lungs were removed, a portion was cultured, and the rest was examined histologically. Of the twenty sensitized rabbits, three that showed no cutaneous sensitivity and three that were only slightly skin-sensitive at the time of intratracheal injection exhibited no detectable pulmonary reaction to the autolysate; eleven of fourteen that showed moderate to extreme cutaneous hypersensitiveness were found to have an acute exudative inflammation of the lungs. The exudate consisted largely of polymorphonuclear leukocytes and serum. It varied in extent from a slight focal exudate lining the bronchioles and adjacent alveoli to a marked diffuse involvement of considerable portions of the lung. In all but one of the eleven cases the cultures of the lungs were sterile. The single animal yielding a positive culture (*Bacterium lepisepticum*) has been excluded. None of the seven nonsensitive controls showed any pulmonary reaction to the autolysate. From these results it may be concluded that there is in rabbits a fairly close parallelism between cutaneous and pulmonary hypersensitiveness to pneumococcus autolysate, and that the inflammatory response of the pulmonary tissue resulting from contact with the autolysate depends on the allergic state of the animal rather than on inherently injurious substances in the autolysate. The observations are in harmony with the theory that allergy may play a part in the pathogenesis of pneumococcus pneumonia in man.

AUTHORS' SUMMARY.

THE DISTRIBUTION OF FRIEDLÄNDER'S BACILLI OF DIFFERENT TYPES. LOUIS A. JULIANELLE, J. Exper. Med. **52**:539, 1930.

In a study of the distribution of the specific types of Friedländer's bacillus, it is shown that, of eighty strains, 52 per cent belong to type A, 15 per cent to type B, 9 per cent to type C and 24 per cent to group X. Type A includes for the most part strains derived from diseases of man, and more than 70 per cent are associated with pneumonia in man. Type B includes the greatest number of strains from animal sources, while the heterogeneous strains comprising group X come from the greatest variety of diseases. It was demonstrated that in a patient with pneumonia due to Friedländer's bacillus (type A) a specific precipitin reaction of the urine occurred in the corresponding (type A) immune serum. A study of the sugar fermentations of Friedländer's bacillus shows that there is no correlation between serologic type and fermentative activity; the fermentation reactions are variable and therefore not reliable for distinguishing Friedländer's bacillus from closely allied organisms; the strains of group X show the greatest variation in fermentation, and of fifteen strains unable to ferment lactose, thirteen belong to type A.

AUTHOR'S SUMMARY.

EXPERIMENTS ON T. LEWISI INFECTION IN ALBINO RATS. DAVID PERLA and J. MARMORSTON-GOTTESMAN, J. Exper. Med. **52**:601, 1930.

Trypanosoma lewisi infection was studied in normal rats by daily quantitative estimates of the trypanosomes in the blood during the course of the infection.

Splenectomized rats, after *T. lewisi* infection, showed an increased mortality of from 30 to 100 per cent due to *Bartonella muris* anemia. This was at the height of the anemia, seven days after splenectomy. After forty-eight days, when the anemia had disappeared, *T. lewisi* infection was more severe than in normal rats. Splenic autotransplantation four weeks prior to splenectomy raised the resistance to subsequent *T. lewisi* infections. Thymectomy shortened the course and lessened the severity of the infection. Bilateral gonadectomy in the adult increased the severity of the infection, and the number of trypanosomes at the height of infection was greatly increased. Unilateral gonadectomy did not influence the infection.

E. DELVES.

BACTERIUM GRANULOSIS IN RELATION TO TRACHOMA. E. B. TILDEN and J. R. TYLER, J. Exper. Med. **52**:617, 1930.

The original culture of Noguchi (Albuquerque 1), after 2½ years of growth on artificial medium, gave positive results on inoculation in about one third of a total of 15 *rhesus* monkeys. The lesions, however, were not progressive and often receded after a few months. Two chimpanzees similarly infected showed only a few follicles which did not progress. *Rhesus* monkeys immunized by subcutaneous or intravenous injection of *Bacterium granulosis* were not protected against subconjunctival infections with emulsions obtained from active conjunctival lesions in the monkey. Transmission of this strain (Albuquerque 1) by passage from eyelid to eyelid in a series of 30 *rhesus* monkeys, an emulsion of conjunctival tissue being used, gave more striking results. The lesions were more severe and lasted a much longer time. With repeated passages of material from the conjunctiva of one monkey to that of another, the incubation period became longer (it rose from 13 to 139 days), and the positive results less frequent. In one experiment, a suspension made from the excised conjunctiva of a monkey (*M. rhesus* 72) with active lesions infected only 1 of 15 monkeys. When several monkeys (4 or 5) were inoculated with a given conjunctival suspension, it was not uncommon for only one of the series to show lesions and occasionally all failed to present them. Pannus never developed. There was no entropion or ectropion. Occasionally the lesions disappeared or remained unilateral. At times monkeys showed no lesions in the inoculated eye and good lesions in the uninoculated one.

Attempts at the isolation of *Bact. granulosis* from active, untreated lesions in man or monkey did not always succeed. Similarly, the organism was not recovered from the secretions of an active infection in a monkey (*M. rhesus* 51).

Six additional strains of *Bact. granulosis* were isolated by the authors from cases of trachoma occurring in the Indian schools of Arizona. The cultures thus obtained were identical morphologically and culturally with those isolated by Noguchi, and induced the same chronic granular conjunctivitis in monkeys. Advanced cases in which treatment had not been given were more favorable for cultural study than cases in which treatment had been begun.

Cultures of *Bact. granulosis* kept on semisolid medium containing 10 per cent rabbit serum ("leptospira medium") remained viable for many months at room temperature, and sealed ampules of such cultures were found to retain their pathogenicity for the conjunctiva of the monkey for at least 69 days at room temperature, and for at least 284 days at from 4 to 6 C.

Several additional cultural and biologic characteristics of *Bact. granulosis* are described. Of outstanding importance is the fact that cocaine, in contradistinction to procaine, had a bactericidal effect on the organism. This fact, in view of the common use of cocaine for anesthesia, may explain the negative results of cultivation experiments reported by some workers.

CHARLES WEISS.

FUNGI ISOLATED FROM SKIN DURING AN EPIDEMIC OF PERLÈCHE. ERNST PRIBRAM, J. Infect. Dis. **47**:1, 1930.

In an epidemic of perlèche, yeast cells were isolated from the skin lesions. Three different types were found and classified: *Mycoderma, Candida* and

Cryptococcus. These types have different characteristics. *Mycoderma* has an unbranched mycelium without conidia; *Candida* has a branched mycelium and ovoid or spherical conidia; *Cryptococcus* has no mycelium and spherical or hexagonal cells without spores. The three types are connected by transition forms, which may be called incomplete or imperfect forms of the *Candida* type. The fermentation of lactose by the majority of the strains suggests an infection by way of milk or cream.

AUTHOR'S SUMMARY.

RINGWORM OF THE SCALP CAUSED BY ALTERNARIA TENUIS NEES. ERNST PRIBRAM, J. Infect. Dis. **47**:11, 1930.

A mold containing a brown pigment and brown spores has been isolated in different epidemics of ringworm of the scalp. It has been identified as *Alternaria.*

AUTHOR'S SUMMARY.

THE TYPES OF TUBERCLE BACILLI FOUND IN TUBERCULOUS LESIONS AND IN NONTUBERCULOUS TISSUE IN MAN. J. D. ARONSON and C. E. WHITNEY, J. Infect. Dis. **47**:30, 1930.

Tubercle bacilli obtained from latent and progressive lesions and from nontuberculous tissue fall into two distinct groups, with occasional atypical strains. The human type of tubercle bacilli is characterized by luxuriant growth on glycerol agar and slight pathogenicity for the rabbit. The bovine type of tubercle bacillus is characterized by sparse growth in early generations on glycerol agar and high pathogenicity for the rabbit. The atypical strains may grow luxuriantly on glycerol agar and be highly pathogenic for rabbits, or the cultures may grow sparsely and be slightly pathogenic for rabbits. The glycerol reaction curve was not found to be specific for the respective types. No difference between the types could be detected by means of the complement-fixation reaction. From latent tuberculous lesions of human autopsy material there were isolated eighty-three cultures of the human type of tubercle bacillus, three of the bovine type and two atypical strains. From progressive tuberculous lesions, ninety-six cultures of the human type and three of the bovine type were isolated. From lung tissue, pulmonary lymph nodes and mesenteric lymph nodes free from tuberculous lesions, there were isolated thirty-eight cultures of the human type and two atypical cultures. Three of the bovine cultures were obtained from guinea-pigs inoculated with material from latent pulmonary tuberculous lesions in patients, aged 42, 65 and 65 years. Three cultures of bovine tubercle bacilli were obtained from the mesenteric nodes of children, aged 10 and 12 months, and from a lung of the second child. The atypical strains of tubercle bacilli were isolated from two patients, aged 57 and 70 years. Two of the cultures were obtained from nontuberculous lesions and two from a latent tuberculous lesion.

AUTHORS' SUMMARY.

THE LOCALIZATION OF STREPTOCOCCI IN THE TISSUES OF RABBITS. EUGENIA VALENTINE and MARTHA VAN METER, J. Infect. Dis. **47**:56, 1930.

The results obtained in this study indicate that the localization of streptococci in the tissues of rabbits following the intravenous inoculation of unpurified mass cultures is not intimately dependent on the source of the specimen or the clinical history of the person furnishing it. Regardless of the origin of the specimens, lesions were found in the joints in 65 per cent of the rabbits, in the muscles in 22 per cent, in the heart in 21 per cent and in the kidney in 18 per cent. Following the injection of two culturally or serologically different varieties of *Streptococcus,* the organisms were found to localize independently in different joints or tissues; or one type was found to invade one rabbit, while the other type predominated in the other animal; or one type, preeminently the green-producing varieties, might invade to the exclusion of the other. In virtually all

instances streptococci isolated from lesions of inoculated rabbits were found to be similar culturally and serologically to those isolated from the original mass culture. Little difference was noted between the invasive capacity of streptococci vegetating on the mucosa of the buccal cavity and those isolated or cultured from acute or chronic apical abscesses. The variation in the susceptibility or resistance of individual rabbits, into which injections of the same culture at the same time in approximately the same dosage were made, is so marked that it is deemed unjustifiable to draw conclusions regarding elective localization from the results obtained by the injection of less than a considerable number of animals per specimen. No evidence of localization of streptococci in the bony structure of the labyrinth of the ear was noted in 100 rabbits examined at autopsy.

AUTHORS' SUMMARY.

PLEOMORPHIC MICRO-ORGANISM ASSOCIATED WITH INFECTIOUS AVIAN LARYNGOTRACHEITIS. ROBERT GRAHAM, FRANK THORP, JR., and W. A. JAMES, J. Infect. Dis. **47**:83 and 87, 1930.

A pleomorphic micro-organism isolated from the laryngeal and tracheal exudates of fowls, naturally infected with acute infectious laryngotracheitis, is a gram-positive, hemolytic, nonmotile, nonspore-bearing, facultative anaerobe, which requires a blood agar medium for its successful cultivation. Morphologically, the pleomorphic micro-organism has coccoid, diplococcoid, ovoid, granular or beaded rod forms suggestive of the diphtheroid group. Subacute or chronic avian laryngotracheitis (a mild form of the acute disease) has been observed in flocks in which other fowls previously (from three to six months) suffered from the acute and fatal type of the disease, as well as in flocks in which a negligible number of acute cases of the disease were simultaneously recognized. The subacute type of the disease can be propagated continuously from fowl to fowl by placing a sterile cotton swab in the larynx of an infected fowl and then in the larynx of a healthy fowl. The acute form of the disease cannot be continuously transferred from fowl to fowl by laryngeal swabs. By this method of exposure, the acute type is transformed into the subacute. The subacute type, by repeated laryngeal transfers, in our experience does not become acute. The subacute or chronic type of avian laryngotracheitis has a low mortality in naturally as well as in artificially induced cases. Clinically, the disease is characterized by mild intermittent symptoms of a low grade inflammation of the larynx and trachea, which consist of shaking the head and rapid intermittent swallowing, with solitary stenotic laryngotracheal sounds or a continuous "wheezing" sound. Normal egg production, color of the comb and appetite are not necessarily altered. Dulness and lack of vigor may be periodically observed in the chronic, subacute type of the disease, followed by emaciation and death. A pleomorphic micro-organism was isolated from fowls naturally infected with the subacute type, as well as from fowls artificially infected by swabs from the acute disease. This micro-organism is pleomorphic and appears indistinguishable from the pleomorphic micro-organism encountered in the acute and fatal form of the disease.

AUTHOR'S SUMMARY.

THE LENGTH OF SURVIVAL OF PARATYPHOID BACILLI IN FOODSTUFFS. L. P. DOYLE, J. Infect. Dis. **47**:92, 1930.

The length of time for which paratyphoid bacilli lived after being introduced into certain canned vegetables varied within wide limits. *Salmonella aertrycke* remained alive in canned spinach for three years. *S. aertrycke* and *S. enteritidis* agglutinogens were easily demonstrated in unheated corn, spinach and peas three years after inoculation. *S. aertrycke* agglutinogens were clearly demonstrable in the vegetables after being heated. Relatively slight heating apparently destroyed or greatly reduced the *enteritidis* agglutinogens.

AUTHOR'S SUMMARY.

PRESENT KNOWLEDGE OF THE ETIOLOGY OF TRACHOMA. CHARLES WEISS, J. Infect. Dis. **47**:107, 1930.

It must not be assumed that even if *Bacterium granulosis* is finally accepted as the cause of trachoma, an end will have been made of this great problem. On the contrary, several new and promising fields of investigation will remain. For example, what is this spontaneous follicular conjunctivitis that occurs among various monkeys, chimpanzees and rabbits? What is its relation to trachoma in man? Is the presence of secretion in trachoma in man due to a mixed, a secondary bacterial or a virus infection? Are there trachoma carriers? And, of course, there will still remain the practical problem of developing specific prophylactic and therapeutic measures against this disease, which now constitutes a serious problem of public health throughout the United States and in nearly all the countries of the world.

AUTHOR'S SUMMARY.

PURE CULTURES OF CLOSTRIDIUM BUTYRICUM IODOPHILUM FROM HUMAN FECES. NANNA SVARTZ, J. Infect. Dis. **47**:138, 1930.

Iodophil clostridia, abundant in intestinal fermentative dyspepsia, were isolated in pure cultures from human feces. The most typical feature of these bacteria was their inclination to form and deposit starchlike, iodophil substance, and to change into clostridial form, two biologic processes that take place according to fixed rules. Comparative experiments with the strains thus isolated and those obtained from other laboratories under the names of *Bacillus amylobacter* and *Clostridium butyricum* showed that the new strains differ from the other strains. Among other tests made were those with agglutinating serum produced against one of the new strains. The comparative tests showed further that the strains of *B. amylobacter* obtained from different laboratories differed also among themselves, and that entirely different bacteria go by the same name. The name *Clostridium butyricum-iodophilum* is suggested for the iodophil clostridium-forming bacterium here described.

AUTHOR'S SUMMARY.

REACTIONS IN GUINEA-PIGS FOLLOWING INOCULATION WITH HEAT-KILLED TUBERCLE BACILLI. ARNOLD BRANCH and J. R. CUFF, J. Infect. Dis. **47**: 151, 1930.

Allergy and anaphylaxis in tuberculosis are independent phenomena, and immunity may be present without allergy. Intramuscular inoculation with heat-killed tubercle bacilli (and probably also intravascular inoculation) produces immunity and anaphylaxis without allergy, whereas intraperitoneal and intrapleural inoculation produces allergy, anaphylaxis and immunity. The development of allergy appears to be interrelated with the process of caseation. The practicability of prophylactic immunization of children by intramuscular inoculation with heat-killed virulent tubercle bacilli is suggested, the advantage being that if immunity can be obtained without allergy a positive reaction in the valuable tuberculin skin test later is evidence of infection and not the result of the vaccination.

AUTHORS' SUMMARY.

MENINGOCOCCUS MENINGITIS IN DETROIT, 1928-1930. JOHN F. NORTON and NORMA H. BROOM, J. Prev. Med. **4**:355, 1930.

During the 1928-1929 epidemic of meningitis in Detroit, sixty-two meningococcus strains were isolated from patients and thirty-three meningococcus strains from carriers (home contacts of the patients). These ninety-five strains were all agglutinated by a polyvalent antimeningococcus serum in a dilution of 1:400. In carbohydrate fermentation reactions, maltose gave the most consistent results, while saccharose fermentation was not uncommon. These cultural tests were less reliable than the serologic tests. Strains isolated from patients (spinal fluid) were, on the

whole, more virulent for white mice than those found in contact carriers (nasopharynx). Agglutination tests with serums prepared with standard group cultures gave unsatisfactory results and did not permit a definite grouping. Agglutination absorption tests showed that the organisms could be assigned definitely to group III. Both agglutination and absorption-of-agglutinin experiments with serums prepared from cases and carrier strains isolated during the outbreak in Detroit and tested against ten cases and nine carrier strains, gave definite evidence of the serologic identity of the organisms involved.

AUTHORS' SUMMARY.

THE TYPE DISTRIBUTION OF MENINGOCOCCI IN THE UNITED STATES DURING 1928 AND 1929. SARA E. BRASHAM, C. E. TAFT and S. A. CARLIN, Pub. Health Rep. **45**:1131, 1930.

One hundred and fifty-five strains of meningococci, isolated during the last eighteen months, have been typed according to the classification of Gordon. Of these, 90.8 per cent fall into Gordon's four groups, whereas 9.2 per cent do not seem to be represented in that classification. Comparison with the grouping during the epidemic years 1918-1919 shows a present greater preponderance of types I and III (which are considered by many to belong to the same group), a definite decrease in type II, a marked increase in type IV, and a decrease in the number of strains that could not be typed. A striking contrast is seen in intervening nonepidemic years in which there was a great predominance of atypical strains.

These studies indicate that at least 90 per cent of the meningococci studied during this last year are typical agglutinogenically, and that they are on the whole fairly well represented in the polyvalent serums prepared for therapeutic use.

HAEMOLYSIN PRODUCED BY ATOXIC STRAINS OF B. TETANI. JOHN C. KERRIN, Brit. J. Exper. Path. **11**:153, 1930.

Atoxic strains of *Bacillus tetani* secrete as powerful a hemolysin as do the toxic strains. Normal serum and cholesterol exert a powerful antagonistic effect against tetanolysin, while lecithin has no antihemolytic power.

AUTHOR'S SUMMARY.

A BACTERIOLOGICAL STUDY IN THE COURSE OF CHOLECYSTECTOMY. G. G. TAYLOR and L. E. H. WHITBY, Brit. J. Surg. **18**:78, 1930.

Intestinal bacteria, rather than streptococci, are regarded as the more frequent cause of infection of the gallbladder. By anaerobic methods *Bacillus welchii* was frequently found in cases of acute cholecystitis and in 9 per cent of the organs examined. The same organism was found in the centers of 13 per cent of gallstones obtained from the autopsy room. The route of invasion is most likely by way of the portal system to the liver and thence by the periportal lymphatics to the gallbladder.

RICHARD A. LIFVENDAHL.

THE AETIOLOGY OF LYMPHADENOMA. C. C. TWORT, J. Path. & Bact. **33**:539, 1930.

The etiology of lymphadenoma (Hodgkin's disease) remains obscure to us. We could consistently demonstrate no specific animal or vegetable parasite in the diseased tissues by direct microscopic examination, by cultivation or by injection into animals, in spite of the numerous artifices adopted. Cultures of antemortem lymphadenomatous glands were in almost all instances sterile, and we were unable to repeat the positive results which many other workers have been fortunate enough to obtain in infection experiments on animals. An assortment of other in vivo and in vitro experiments gave absolutely barren results; in fact so invariably did the different experimental procedures which we adopted lead to nothing that one

might have been dealing with a true new growth instead of what is generally accepted to be a granuloma.

AUTHOR'S SUMMARY.

BACTERIOPHAGE REACTIONS OF FLEXNER DYSENTERY STRAINS. F. M. BURNET and M. MCKIE, J. Path. & Bact. **33**:637, 1930.

Bacteriophages active against Flexner dysentery bacilli can be subdivided according to Bail's methods into four main groups. One of these groups comprises phages capable of lysing only the smooth phase; phages of the other three may or may not lyse smooth strains, but, with an occasional exception, lyse rough forms of all the Flexner types. Two of the latter groups are homologous with similar groups of *Salmonella* bacteriophages. The various Flexner types, V, W, X, Y, Z of Andrewes and Inman, present characteristic differences in their phage sensitivity. Antigenically similar strains show practically identical reactions toward a series of phages.

AUTHORS' SUMMARY.

INFECTIOUS ECTROMELIA. J. MARCHAL, J. Path. & Bact. **33**:713, 1930.

A natural disease occurring in a breeding stock of mice has been described. This was characterized by high mortality in the stock and, in a minority of the sick animals, by a local lesion, usually the swelling of one hind foot, which in some mice was followed by gangrene and separation of the gangrenous portion; these mice often recovered. Animals dying without local symptoms showed, on postmortem examination, definite lesions of the liver and spleen. This disease was considered to be due to a filter-passing virus for the following reasons: Emulsions of certain organs and some body fluids proved to be infective, even in very high dilution, although there was no evidence of the presence of any bacteria. Bacteria isolated from the local lesions or internal organs did not reproduce the disease, even when large doses were given. Emulsions of the liver and spleen or other infected tissue filtered through candles (Pasteur-Chamberland L2, Mandler and Berkefeld N) capable of holding back bacteria proved to be highly infective. Histologic examination showed that the outstanding feature of the action of the virus was necrosis, which especially affected the mesoblastic tissues. Epithelial tissues, when attacked, showed cytoplasmic inclusion bodies with strongly acidophil staining reactions. At low temperature, from 0 C. to —10 C. the virus could be preserved for long periods. Infected tissue preserved either in 50 per cent glycerin or pure glycerin and stored at 0 C. remained active for months. Infected tissue dried over phosphorus pentoxide and stored at room temperature showed no loss of virus at the end of six months. At 50 C. the infectivity was not entirely inactivated in two hours; at 55 C. it showed complete inactivation in thirty minutes. Phenol 0.5 per cent did not inactivate it even after fifty days; phenol 1 per cent had not rendered emulsions of liver noninfective after twenty days. Formaldehyde 0.01 per cent completely inactivated the virus after forty-eight hours. An attack of the disease rendered the animal solidly immune to the injection of many lethal doses of the virus. Serum obtained from convalescent animals neutralized the effect of the virus when mixed with it before injection.

AUTHOR'S SUMMARY.

INTRAOCULAR INJECTION OF VIRUS OR TSUTSUGAMUSHI DISEASE AND TYPHUS FEVER. M. NAGAYO and others, Jap. J. Exper. Med. **8**:309 and 319, 1930.

The virus of tsutsugamushi disease and the virus of typhus fever were inoculated separately into the eye in rabbits and guinea-pigs. In both cases, minute microbic forms were found in Descemet's membrane, and the organisms and lesions corresponded to those in patients and in otherwise infected animals. Neither virus produced changes in the eye, and no organisms were demonstrated in immune animals. Attention is called to this method for studying other viruses.

BACTERIAL HAEMOTOXIN. K. NAGASE, Jap. J. Exper. Med. **8**:379, 1930.

After purification, the hemotoxin of *Vibrio El Tor* showed no protein reactions and contained only a small amount of nitrogen. The purified, like the nonpurified, hemotoxin produced a specific antihemotoxin. Fermentations indicate that the hemotoxin is not a protein, but may be of the nature of a carbohydrate. The streptococcus hemotoxin was found to have similar properties.

TRANSMISSION OF THE SPIROCHETES OF RECURRENT FEVER BY TICKS. CHARLES NICOLLE, CHARLES ANDERSON and JACQUES COLAS-BELCOUR, Arch. Inst. Pasteur de Tunis **19**:133, 1930.

An entire number of the journal, ninety-seven pages, is devoted to the compilation and orientation of published and unpublished work done since 1926 at the Pasteur Institute of Tunis on the subject of the transmission of spirochetes by ticks. Ten recurrent fever viruses and five species of *Ornithodorus*, from various sources, have been used. Following a brief discussion of the nymph stage in the life of ticks, concise experimental data are presented. The final pages of summary and general conclusions bring out these points:

Although the hosts of the spirochetes vary in their susceptibility to infection, there exists a general indifference among the ticks to the species of spirochete carried. Ticks will harbor spirochetes from regions in which previous contact, outside the laboratory, could not have occurred.

The life of the tick does not exceed twenty months when it is kept in the laboratory and fed regularly. Spirochetes may be harbored as long as from seventeen to twenty months. The males may not, in this respect, react similarly to the females.

A general rule may be stated, that the *Ornithodorus*, in the adult form, does not transmit infection by biting, but in the nymph stage does so until the adult stage is reached. There are exceptions, based on the life habits and environment of the ticks. A lapse of time is necessary after ingestion before infection is possible. The infecting stages may be maintained for five or six months—exceptionally, for fifteen months. Repeated infection of the tick does not appear to result in immunity.

Ticks infected per ovum are somewhat less constant in their capacity to infect the vertebrate host than ticks infected by ingestion. Hereditary transmission to the first generation is somewhat irregular, to the second rare and to the third never observed. This is true regardless of whether the tick-spirochete relationship is natural or foreign.

Preservation of the virus involved the factors of hereditary transmission and length of life in the ticks, and the frequency of contact with hosts suited to both tick and virus. Man is only an accidental factor in the chain.

The natural route of inoculation, ingestion, seems to afford the best opportunities for the spirochete cycle within the tick. Ticks otherwise inoculated were less frequently infected, and the virus survived a shorter time.

Although the natural vector, the tick, may be infected with spirochetes foreign to them in nature with no apparent difference in reaction, adaptation to other invertebrates of somewhat similar habits, such as lice, which might serve as vectors, is seldom successful. Conversely, adaptation to the tick of viruses normally not transmitted by the tick is seldom, if ever, accomplished.

There is danger of becoming lost in detail. Histologic studies of the ticks need amplification, but this may be done at a later period; material might be available to carry this study to some distant time. Studies of factors of sex in infection and careful observations on given lots of the *Ornithodorus*, rather than on exemplary individual ticks, are needed.

M. S. MARSHALL.

EXPERIMENTAL INVESTIGATIONS OF MIXED INFECTIONS. J. BÜRGERS, Klin. Wchnschr. **9**:1666, 1930.

When injected into guinea-pigs, streptococci did not increase the virulence of diphtheria bacilli; on the contrary, diphtheria bacilli increased the virulence of

the streptococcus. In mice the results were different; when nonlethal doses of diphtheria bacilli with half the lethal dose of a streptococcus culture were injected intraperitoneally, the animals died rapidly from a double infection. In other experiments it was demonstrated that diphtheria toxin does not increase the virulence of streptococci. Streptococci definitely increase the virulence of *B. influenzae* when injected together (subcutaneously or intraperitoneally). Likewise, on subcutaneous injection, influenza bacilli definitely increase the virulence of streptococci. Experiments with type I pneumococcus showed that the virulence is increased threefold by simultaneous injection of *B. influenzae*. The virulence of the influenza bacillus can also be increased fourfold by the simultaneous injection of pneumococci. The investigations were extended to include the saprophytes. It was shown that diphtheria or streptococcus toxin made *B. prodigiosus, B. vulgatus* and *B. subtilis* virulent, as did sublethal doses of streptococci.

CHARLES WEISS.

THE BACTERIAL FLORA OF ULCUS CRURIS VARICOSUM. KARL BAERTHLEIN, Zentralbl. f. Bakteriol. **114**:1, 1929.

This paper contains a detailed, tabulated analysis of the bacteriologic observations in varicose ulcer of the leg. The bacterial flora of the ulcer in 320 patients, was studied, smears and cultures being made in each case. For the latter, Loeffler's medium, ascitic agar and litmus lactose agar were used.

Of the 320 cases examined, staphylococci were present in 308, diphtheria and diphtheroid bacilli in 178, *Bacillus coli* in 98, streptococci in 66, *Bacillus proteus* in 25, *Bacillus pyocyaneus* in 22 and in a few cases, spirochetes, fusiform bacilli, yeasts, pneumococci, *Bacillus prodigiosus* and sarcinae were found.

The author considers that many of the diphtheria bacilli found were pathogenic, and in one patient he believes that symptoms of generalized toxemia resulted from their action. In this patient, an autogenous vaccine seemed to relieve the symptoms.

Baerthlein believes that the bacterial infection of varicose ulcer should not be regarded as that of harmless saprophytes but of definitely pathogenic micro-organisms. Consequently, antiseptic therapy and particularly autogenous vaccine therapy should be applied. For the vaccine, the mixed growth, suspended in saline solution and heated at 56 C. for one hour should be used.

PAUL R. CANNON.

THE RETICULO-ENDOTHELIAL SYSTEM IN INFECTIOUS JAUNDICE. R. S. TSCHERIKOWER and P. L. RUBINSTEIN, Zentralbl. f. Bakteriol. **114**:65, 1929.

The authors infected twenty-five splenectomized guinea-pigs and twenty-one controls with a weakly virulent strain of *Spirochaeta icterogenes* Verdun. Eight of the former and five of the latter died of infectious jaundice; therefore, no significant difference was evident as a result of the splenectomy.

PAUL R. CANNON.

THE CURE OF WEIL'S DISEASE IN GUINEA-PIGS AFTER TREATMENT WITH BISMUTH-YATREN. A. P. UHLENHUTH and W. SEIFFERT, Zentralbl. f. Bakteriol. **114**:241, 1929.

The authors confirmed their earlier results that Weil's disease in guinea-pigs may be prevented by treatment, within five days after percutaneous injection of the spirochetes, with bismuth-yatren. Furthermore, six weeks later the animals injected with the bismuth were found to be spirochete-free, as revealed by the injection of organ-emulsions into other guinea-pigs. Animals treated with a preparation containing a bismuth compound and chiniofon were immune to reinfection several weeks later and contained protective immune bodies in their serums. The authors believe, from an analysis of the data, that the therapeutic effect is not a direct spirocheticidal one, but that the bismuth acts on the defense mechanism of the infected animals, thereby securing an increased response to the infecting micro-organisms.

PAUL R. CANNON.

Immunology

SKIN REACTIONS TO DIROFILARIA IMMITIS IN PERSONS INFECTED WITH WUCHERERIA BANCROFTI. WILLIAM H. TALIAFERRO and WILLIAM A. HOFFMAN, J. Prev. Med. **4**:261, 1930.

A large proportion of persons infected with *Wuchereria bancrofti* exhibited an immediate positive skin reaction to the intradermal injection of about 0.025 cc. of a 0.5 per cent saline extract of dried, powdered *Dirofilaria immitis*. Control tests with other parasitic extracts gave negative results. The possession of pseudopods by the urticarial wheal was used as the criterion of positiveness. In this way, twenty-three persons known to be infected with the germ showed nineteen positive reactions; fifty-six persons possibly infected showed thirty-eight positive reactions; twenty-two persons probably uninfected showed one positive reaction, and nineteen persons known to be uninfected showed no positive reactions. In another series of experiments in which the criterion of positiveness was determined by the possession of pseudopods by the wheal, or a wheal 10 mm. or larger in diameter with a concomitant negative reaction to some other parasitic extract, the twenty-three persons known to be infected showed twenty-one positive reactions; the fifty-six persons possibly infected showed forty-six positive reactions; the twenty-two persons probably uninfected showed one positive reaction, and the nineteen persons known to be uninfected showed no positive reactions. There seemed to be no correlation between age and reactivity either among infected persons or in the whole group of infected and noninfected persons. In five of eleven cases, sensitivity was passively transferred to a local area in the skin of nonsensitive persons by the injection of serum from a sensitive person ("local passive transfer"). In contrast to the immediate reaction, few persons infected with *Wuchereria bancrofti* exhibited delayed reactions to intradermal injections of extracts of *Dirofilaria immitis*. Thus, of twenty-three persons known to be infected, only three exhibited marked delayed reactions; of thirty-nine persons possibly infected, two gave marked, four slight and three doubtful positive reactions; of twenty-two persons probably uninfected five gave very doubtful reactions, and of twenty-one persons known to be uninfected four showed very doubtful reactions.

AUTHORS' SUMMARY.

THE UNION OF VACCINE VIRUS AND ITS SPECIFIC ANTI-SERUM IN VITRO. N. E. MCKINNON, J. Prev. Med. **4**:411, 1930.

Experiments are presented that indicate that vaccine virus forms stable union in vitro with its specific antiserum, and that a certain duration of contact is required to effect the stability of the union. This is confirmatory evidence that the union of vaccine virus and its specific antibody is comparable to other antigen-antibody unions, without the intervention of alexin (complement). A question is raised in regard to the significance and interpretation of the dilution phenomenon. Perhaps the difference between these observations and those reported from other laboratories is due to the fact that dermal vaccine was used in the experiments here reported.

AUTHOR'S SUMMARY.

IMMUNOLOGIC DIFFERENTATION OF PALLIDA STRAINS. F. PLAUT and H. KASSOWITZ, Klin. Wchnschr. **9**:1396, 1930.

Identical immune serums as tested by agglutination, spirocheticidal effect and complement fixation were obtained by the immunization of rabbits with cultures of two pallida strains and with pallida autolysates. These two strains differed immunologically from a third strain.

AUTHORS' SUMMARY.

IMMUNOLOGIC CORRELATIONS BETWEEN HERPES SIMPLEX AND VACCINIA. H. PETTE, Zentralbl. f. Bakteriol. **114**:185, 1929.

Rabbits were given injections intracorneally with herpes virus, and the brain and cord were subsequently studied, both in normal rabbits and in others pre-

viously given injections intracutaneously or intracorneally into the other eye with vaccine virus. No immunity of any significant degree was found to result from previous treatment with vaccine virus. Also, the herpes encephalitis was uninfluenced in its histologic character by previous vaccination with vaccine virus.

PAUL R. CANNON.

IMMUNITY IN EXPERIMENTAL SPOTTED FEVER. YOSHIAKI FUKUDA, Zentralbl. f. Bakteriol. **115**:83, 1929.

Fukuda studied the effects in guinea-pigs of infection with the virus of spotted fever and observed an active immunity in each case in which the previous infection had been a normal, febrile one. The simultaneous injection of immune serum and virus caused a symptomless infection to develop, which, however, conferred an active immunity. He demonstrated that the virus develops in the symptomless infection, but that it is somewhat restrained by the immune serum.

PAUL R. CANNON.

THE RELATIONSHIP BETWEEN INHIBITING SUBSTANCES FOR TUBERCLE BACILLI AND TUBERCULIN ALLERGY. M. SONAK, Zentralbl. f. Bakteriol. **115**:173, 1930.

Sonak mixed 10 cc. of blood and 2.5 cc. of a freshly prepared suspension of human tubercle bacilli in a paraffined Wright capillary tube, sealed the tube in a nonparaffined capillary pipet and incubated it at 37 C. Shreds of the blood were then placed on sterile slides and incubated for nine days more, at the end of which time these were suitably prepared and stained to demonstrate the groups of tubercle bacilli that had grown. The results indicated a pronounced inhibition of growth in blood from children giving positive reactions to the tuberculin, while growth was favored in blood from children with measles taken during and shortly after the exanthem, as well as in two children giving negative reactions to the tuberculin.

PAUL R. CANNON.

ORGANOSPECIFIC ELEMENTS IN BRAIN TISSUE. E. WITEBSKY and G. SALLAZZO, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:1, 1930.

Organospecific antibrain serum reacts in the brains of guinea-pig and human embryos. The reacting elements of the embryonal brain tissue are designated as "lipoids."

THE ACTION OF PHENOL ON THE ANTIGENIC PROPERTIES OF DIPHTHERIA TOXIN. L. TSCHERTKOW, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:25, 1930.

Phenol (0.5 per cent) weakens the antigenic powers of diphtheria toxin more rapidly than toluene.

BLOOD GROUPS IN ANIMALS. O. THOMSEN and T. KEMP, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:251, 1930.

The blood corpuscles of rabbits contain receptors that bind human anti-B agglutinin. In many rabbits the serum contains anti-A agglutinin for human corpuscles. Monkeys frequently have receptors for human anti-B agglutinin.

EXPERIMENTS WITH DIPHTHERIA ANATOXIN. M. P. ISABOLINSKY and V. I. GITOVITSCH, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:441, 1930.

Guinea-pigs were immunized by anatoxin not only against diphtheria toxin, but against diphtheria bacilli in pure cultures.

ANTIBODIES AGAINST LEUKOCYTES. E. WITEBSKY and K. KOMIGA, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:480, 1930.

Leukocytes from guinea-pigs injected into rabbits led to the production not only of Forssman's heterogenetic antibodies, but antibodies against alcoholic extracts of guinea-pigs' leukocytes and spleen. In the rabbit species leukocytes from rats produced specific lipoid antibodies, the action of which was not, however, limited to the leukocytes.

THE EFFECT OF A TUBERCULOUS FOCUS ON THE IMMUNE REACTIONS OF THE BODY. L. DIENES, Ztschr. f. Immunitätsforsch. u. exper. Therap. **68**:13, 1930.

In experiments on rabbits it was found that the introduction of antigen into a local focus produced more marked results than intravenous injection into animals with similar foci. The removal by operation of the focus within a few hours after the injection of the antigen had no effect on the result. It is not possible to explain this result at the present time.

THE CHEMICAL NATURE OF THE HETEROGENETIC ANTIGEN IN SHIGA BACILLI. KURT MEYER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **68**:98, 1930.

The carbohydrate fraction isolated from *Shiga* strains, which contain heterogenetic antigen units with the corresponding heterogenetic antibody. The heterogenetic antigen in *Shiga bacilli* is regarded as a carbohydrate.

ARRANGEMENT OF ENTEROCOCCI INTO TYPES. KURT MEYER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **68**:109, 1930.

Ten strains of enterococci cultivated for more than ten years retained, with one exception, the original type of agglutination. Of sixty-eight new races, approximately 41 per cent could be arranged into four groups according to agglutination and complement fixation. As a rule, the results of agglutination and complement fixation agreed.

PURIFICATION OF HEMOLYSIN. H. VON EULER and E. BRUNIUS, Ztschr. f. Immunitätsforsch. u. exper. Therap. **68**:124, 1930.

By the absorption of a lysin against sheep blood with the stroma of sheep corpuscles and subsequent treatment with ammonia, a purified lysin of high titer was obtained.

Tumors

PRIMARY CARCINOMA OF THE FALLOPIAN TUBES. R. E. WATKINS and W. M. WILSON, Surg. Gynec. Obst. **51**:125, 1930.

The lumen of the distal half of the right fallopian tube was replaced by a hemorrhagic, papillomatous, carcinomatous, oval tumor measuring 5 by 6 cm., which was surrounded by a tubal wall that contained lymphocytes, hypertrophied muscle fibers and tumor cells that had not invaded the serosa. The proximal portion of the tube had a patent lumen permitting a watery, blood-tinged fluid to escape into the vagina. The fimbriated end was occluded except for a small cyst containing a clear serous fluid. The frequent etiologic factors recorded in 200 authenic cases were lacking in this patient in that there were no evidences of long-standing pelvic inflammation. She had had ten full term pregnancies and no miscarriages, there were no wolffian remnants in the tube and subjacent structures, or any para-ovarian new-growths.

RICHARD A. LIFVENDAHL.

CLASSIFICATION OF FOUR THOUSAND EXPERIMENTAL OIL AND TAR SKIN TUMORS. C. C. TWORT and J. M. TWORT, Lancet **1**:1331, 1930.

The following tabulation briefly summarizes one portion of the classification:

	Animals Used	Benign Tumors	Malignant Tumors
Coal gas tars	800	93	106
Synthetic tars	8,800	1,086	1,281
Shale oils	10,000	977	307
Petroleum oils	6,100	183	43
Other oils	500	0	0
Pure compounds	2,900	15	6
Totals	29,100	2,354	1,743

Mice were used in the work, and the types of tumors encountered were classed as arising from (*a*) the surface epithelium, (*b*) the follicular epithelium, (*c*) the sebaceous glands, (*d*) the connective tissue and (*e*) those composed of mast cells. The number of each of these tumors is not stated.

GEORGE RUKSTINAT.

A CONGENITAL DIVERTICULAR RHABDOMYOMA OF THE BLADDER. CHARLES HUETTE, Ann. d'anat. path. **6**:267, 1929.

A detailed description is given of a rhabdomyoma in the bladder of a child 13 months old. The case reported is the sixth; only five have been previously described.

B. M. FRIED.

A STUDY OF MELANOTIC TUMORS. F. ROULET, Ann. d'anat. path. **6**:489, 1929.

Roulet affirms that melanotic tumors should not be classified according to their histogenesis. A cutaneous nevus, during its malignant transformation, is composed of two elements: nevus cells in a state of proliferation and the skin epithelium in a state of malignant segregation. The histologic picture of the tumor will depend on the preponderance of one or the other process. The nevus cell is a desmoplastic element which has lost its epithelial characteristics to acquire connective tissue functions. It is not its blastodermic origin which characterizes it but its virtual histofunctional differentiation. A pigmented nevus of the skin will develop into a tumor with sarcomatous as well as carcinomatous characteristics. According to histofunctional differentiation of the neoplastic cell, one will then speak of sarcomatous or carcinomatous malanoma or of melanosarcoma and melanocarcinoma, disregarding the blastodermic origin of the neoplastic element. The article contains a comprehensive review of the literature on this subject and reports of eight personal cases. A large bibliography is appended.

B. M. FRIED.

EMBRYOMAS IN THE EVOLUTION OF CHORIOCARCINOMA. LOUIS DE WALSCHE, Arch. internat. de méd. expér. **5**:557, 1930.

A case of choriocarcinoma, occurring in a virgin, 16 years of age, is reported. A tumor, diagnosed after operative removal as embryoma, was found in the right posterior culdesac, partially embedded in the corresponding broad ligament. At autopsy, numerous metastases were found in the lungs, pleura, mediastinum, diaphragm, liver and mesentery. The uterus was normal. Microscopic examination of the metastases revealed tissue having the appearance of normal placenta, with syncytium and cells of Langhans. A comprehensive review of the literature is given.

J. N. PATTERSON.

PAGET'S DISEASE OF THE NIPPLE: AN EPIDERMOTROPIC CANCER. C. SIMARD, Bull. Assoc. franç. p. l'étude du cancer **19**:50, 1930.

The diagnosis of Paget's disease of the nipple is made when peculiar, large, clear cells are found at the level of the epidermis. The discussion is centered

around the origin of these cells. Some observers believe that they result from a diskeratosis of the cutaneous layer, while others state that they have migrated to the skin from a preexisting mammary epithelioma. Simard is in favor of the latter opinion. He found morphologic similarities between the cells in Paget's disease and the cells in cases of migrated intramammary cancer. He observed cancers which had recently invaded the epidermis showing all the histologic traits of Paget's disease. And finally, in his experience, all of the clinical cases of Paget's disease of the nipple showed intramammary cancers. His arguments are supported by a detailed study of four cases of clinically diagnosed Paget's disease of the nipple and of six cases of intramammary cancer which had invaded the skin. Experiments with grafting cancer in the breasts of mice likewise supported his observations made on human subjects.

B. M. FRIED.

CHRONIC CYSTIC MASTITIS. C. A. HELLWIG, Arch. f. klin. Chir. **159**:763, 1930.

Of 121 specimens from operations on the breast, 63 showed the changes typical of chronic cystic mastitis. Thirty-five were grouped as simple chronic mastitis, 2 as chronic cystic mastitis with marked epithelial proliferation and 3 as chronic cystic mastitis with atypical proliferation. Twenty specimens showed a combination of chronic cystic mastitis and carcinoma. The initial stages of chronic cystic mastitis are found in one third of all women over 40 years of age, according to autopsy determinations; on the other hand, half of the author's cases of cancer of the breast show cystic changes in the surrounding breast tissue. The opinion of those who regard chronic cystic mastitis as precancerous lesions and advise radical operation is rejected. The irregularity of the intraductal epithelial proliferation was so marked that a radical operation was advised. In only 3 of 40 cases, in which an infiltrating growth could not be found microscopically. Bleeding from the nipple is not a sign of malignancy, for it is observed also in benign lesions. The Wilson method of staining unfixed frozen sections with methylene-blue (methylthionine chloride, U. S. P.) proved reliable in the cases in which biopsy was performed during operation.

AUTHOR'S SUMMARY

THE GROWTH OF METASTATIC TUMORS OF THE BRAIN. R. NISHII, Frankfurt. Ztschr. f. Path. **40**:1, 1930.

This paper deals with the reaction of the tissue of the brain toward metastatic tumors. As a result of an investigation of six cases of metastatic carcinoma and five cases of metastatic sarcoma, the author concludes that the type of cellular reaction of the tissue of the brain is not essentially different in carcinoma and sarcoma. In the majority of cases, however, the metastatic carcinoma does not produce a marked reaction in the surrounding stroma, while the metastatic sarcoma is frequently surrounded by zones of softening or hemorrhage. The reaction of the brain is directed, first, against the infiltrating elements of the tumor, and second, against the mechanical compression of the tumor. The brain reacts toward the mechanical compression with the formation of glia fibers, connective tissue fibers, blood vessels and mast cells. Hemorrhages, necrosis and metabolic changes of the surrounding cells are caused by the invasion of the tumor. The question also is raised whether or not a metastatic sarcoma might cause a blastomatous transformation of the mesenchymal tissue.

CARCINOMA OF THE THYROID WITH EXTENSION INTO THE RIGHT AURICLE BY INVASION OF VEINS. N. J. WYLEGSCHANIN, Frankfurt. Ztschr. f. Path. **40**:51, 1930.

A woman, aged 50, had marked edema and cyanosis of the face. On section, a large portion of the thyroid was found to be replaced by a tumor that occupied almost the entire left lobe, the isthmus and a part of the right lobe. Both superior and inferior thyroid veins, both jugular veins and the subclavian and innominate

veins were filled with tumor thrombi that extended into the right atrium. The tumor consisted of epithelial cells arranged in masses and separated from one another by fibers of connective tissue. There was a slight tendency toward the formation of glandular structures throughout the tumor. In some portions the cells were arranged about blood vessels so as to resemble pictures seen in perithelioma. Many tumor cells were encountered in the veins in the sections of the thyroid as well as in the sections of the larger veins and those of the atrial cavity.

HYPERNEPHROMA-LIKE TUMOR OF THE LEFT SUPRARENAL WITH METASTASIS TO THE LIVER AND APLASIA OF THE RIGHT SUPRARENAL. A. SCHLÜTER, Frankfurt. Ztschr. f. Path. **40**:97, 1930.

The case of a woman, aged 33, is described. The menses had stopped about five years before death. The blood pressure varied from 170 systolic and 110 diastolic to 210 systolic. At autopsy, an abundance of subcutaneous fatty tissue was present, in some portions measuring 5, in other portions 9 cm. in thickness. In the axilla and around the pubic region, only a few hairs were found. There was a tumor, 5 by 8 by 11 cm. in the region of the left suprarenal gland, apparently replacing it, with metastasis into the liver. Histologically, the tumor consisted of large vesicular cells, partly polygonal, lightly stained and arranged into columns resembling those found in the fasciculate zone of the suprarenal cortex. No chromaffin or ganglion cells could be demonstrated. No evidence of medulla was seen within the tumor. The right suprarenal gland was absent. The ovaries showed marked fibrosis and atrophy, with complete disappearance of the follicles. The hypophysis offered an increase in eosinophilic cells with some decrease in basophilic cells. In explanation of the high blood pressure, the theoretical possibility is discussed of an overproduction of epinephrine by an overcompensation of the chromaffin system outside of the suprarenal glands, because of the aplasia of the right suprarenal and the absence of chromaffin cells within the tumor. The atrophy and fibrosis of the ovaries are taken as sequels to the tumor in the suprarenal gland, while the cessation of the menses and the generalized adiposity are believed to be signs of the incompetency of the ovaries.

CARCINOMA IN REGENERATING LIVER TISSUE. P. KOTLJARTSCHUK, Frankfurt. Ztschr. f. Path. **40**:118, 1930.

This article reports the case of obliterating endophlebitis of the hepatic veins which led to an atrophy of a large portion of the liver. These changes caused a regenerating hyperplasia in the tissue of the liver, which in some portions was the seat of a carcinoma. Histologically, the tumor showed small cells that varied in size. The nuclei were large, some lightly stained, others rich in chromatin. No tendency toward the formation of acini was noted. Some necrosis and hemorrhage were found throughout the tissue.

EFFECT OF RADIUM IRRADIATION ON CARCINOMA. J. WÄTJEN, Virchows Arch. f. path. Anat. **275**:156, 1930.

The effects of radium on the tissues of malignant tumors are difficult to determine because they are not readily distinguished from the changes that occur spontaneously in tumors. The examination of bits of human neoplasms removed by biopsy at intervals after irradiation is not satisfactory, because the biopsy procedure itself may cause regressive changes in the tissue, and because the small pieces that are thus removed do not permit the study of sufficiently large areas of tissue. The time of the appearance and the nature of the changes that may be ascribed to radium have been especially difficult to determine. Perthes was able to detect no change in tissue removed from a carcinoma of the breast on the seventh day after irradiation, although in another piece of tissue removed changes were evident on the seventeenth day. Wätjen had the opportunity of studying microscopically the tissues of four patients who died in from one to six

days after the application of radium. All were elderly women, and in each the tumor was a carcinoma of the uterus. In each case, the radium was applied in the same institution, the dosage and filtration were approximately identical, and necropsy was done shortly after death. In one patient, hysterectomy for carcinoma of the body of the uterus had been done five years before death. Two months before death and again on the day before death, radium had been applied intravaginally for pelvic recurrence. Death resulted within twenty-four hours of the second application from pulmonary embolism. A second patient with squamous cell carcinoma of the cervix received two applications of radium within the cervical canal in the course of one and a half days. Two days after the second application stormy symptoms of pulmonary embolism developed when the radium capsule was removed. A pulmonary embolus was not found at necropsy. The third patient, also with squamous cell carcinoma of the cervix, received two intracervical applications of radium and died of pulmonary embolism three days after the beginning of the second application and six days after the beginning of the first application. In the fourth patient, a carcinoma of the body of the uterus was removed by curettage, and radium was inserted into the uterine cavity. Fever developed the next day, and death occurred on the fifth day. In the last case, no tumor tissue could be found within the uterus at necropsy, but the uterine tissue was freshly necrotic at the site of the application. An acute inflammatory reaction extended through the wall of the uterus and involved the covering serosa. In the other three cases, histologic changes are described in the tumor tissue that are held to be the immediate effects of radium. The earliest process noted was cessation of mitosis in the tumor cells. The nuclei revealed evidences of degeneration, and the tumor cells became necrotic. The regressive changes were most marked immediately beneath the site of application of the radium. These alterations Wätjen believes can be differentiated from the spontaneous regressive changes occurring in other parts of the tumor. The vessels of the tumor stroma about the areas of parenchymal necrosis due to radium were engorged and contained an increased number of leukocytes, and the stroma itself was sometimes infiltrated by leukocytes. The stroma reaction, the author believes, is secondary to the changes caused by the radium in the tumor parenchyma, and not due to the action of the radium directly on the stroma itself. Wätjen points out that the application of radium in elderly persons is not without danger. When applied within the uterus, and especially after curettage, he believes that it may lead to bacterial invasion of the tissue with resulting thrombosis, and to death from infection or pulmonary embolism.

O. T. SCHULTZ.

THE RESPONSE OF BLOOD VESSELS TO EXTRACTS OF TUMORS. M. LAPIDARI, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:159, 1930.

The isolated vessels of tumorous chickens, rats and mice respond more actively to the extracts of the homologous tumor than do the vessels of normal animals.

COMPLEMENT-CONTAINING ANTIBODIES IN PATIENTS WITH CANCER AND IN PREGNANT WOMEN. L. HIRSZFELD and W. HALBER, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:286, 1930.

In a large percentage of patients with cancer complement-binding antibodies were found that reacted with alcohol soluble extracts of cancer tissue. In 60 per cent of pregnant women, the serum was found to react with the cancer extracts.

THE DEMONSTRATION OF SPECIFIC ANTIGENS IN CANCER TISSUE. H. LEHMANN-FACIUS and T. TODA, Ztschr. f. Immunitätsforsch. u. exper. Therap. **67**:373, 1930.

When suspensions of carcinomatous tissue, boiled for half an hour at 100 C., were injected into rabbits, the serum acquired the power of elective fixing complement in carcinoma cells.

Medicolegal Pathology

DISTRIBUTION OF ARSENIC IN THE BODY. S. BLUMENFELDT, Deutsche Ztschr. f. d. ges. gerichtl. Med. **15**:501, 1930.

A study to establish the amount of arsenic in various organs, ingested at various times was undertaken. By comparing the quantities of arsenic in the gastro-intestinal canal with those obtained from the analysis of the liver, one cannot draw a definite conclusion as to whether a certain amount of arsenic was administered in one or more doses. In cases in which arsenic poisoning is suspected, one should examine chemically not only the internal organs but the hair, since arsenic will be found in the hair even when the stomach does not show any traces. Instances in which arsenic is found in relatively large quantities in the gastric contents while it is completely absent in the hair, prove to be cases of acute arsenic poisoning. Should the hair contain more arsenic than the stomach, one can conclude that one or more doses of the poison were ingested at some time prior to death. Presence of arsenic in the hair and in comparatively large amounts in the stomach proves conclusively that arsenic was given at different times. Only from the comparison of detected quantities of arsenic in the hair and in the gastric contents is one able to conclude whether the poison was administered once or several times.

E. L. MILOSLAVICH.

AN UNUSUAL OBSERVATION IN AN EXHUMED, PUTREFIED BODY. B. PUCHOWSKI, Deutsche Ztschr. f. d. ges. gerichtl. Med. **15**:532, 1930.

At the autopsy of a man, aged 20, whose body was disinterred two months after death because poisoning was suspected, numerous small, round, yellowish-white nodules, the size of a pinhead, were scattered on the cut surfaces of the lungs. Similar nodules were found on the endocardium and valves as well as between the chordae tendineae. The chemical and microscopic examinations disclosed that these tiny bodies were chiefly of mineral character (calcium phosphate, calcium carbonate) and contained also traces of fat, endothelial cells, and cocci and rod-shaped bacilli. Similar formations may occur on the mucous surface of the intestines. These nodular, mineral deposits are the result of putrefaction.

E. L. MILOSLAVICH.

BLOOD GROUPS IN PATERNITY CASES. KNUDT SAND, W. MUNCK and J. G. KNUDTZON, Deutsche Ztschr. f. d. ges. gerichtl. Med. **15**:535, 1930.

This is a report of the first 500 cases of questions of paternity in which determinations of blood groups were made at the medicolegal institute of the University of Copenhagen.

SUICIDE BY STRANGULATION. P. FRAENCKEL, Deutsche Ztschr. f. d. ges. gerichtl. Med. **15**:564, 1930.

The author describes in detail two cases in which self-strangulation was committed in an unusual manner. In the second case, cataleptic rigor mortis occurred and illustrated the mechanism of the strangulation, viz., the position of the hand holding the loose ends of the cord.

E. L. MILOSLAVICH.

Technical

THE NATURE OF THE GRAM COMPOUND. ALLEN E. STEARN and ESTHER WAGNER STEARN, J. Bact. **20**:287, 1930.

The cell wall theory of the Gram reaction in its ordinary form necessitates the existence in the decolorizer solution of large dye-mordant molecules. Absorption spectrums indicate the presence of only free dye and free iodine in

solutions of methyl violet-iodine precipitate in both alcohol and acetone. The boiling point elevation of a solution of methyl violet-iodine precipitate in acetone indicates complete dissociation into iodine and dye. These observations indicate a high degree of improbability for the ordinary cell wall mechanism for the Gram reaction, but they are in no way contradictory to the chemical mechanism formerly proposed by the authors. Results also indicate that through chemical treatment and starvation the bacteria gradually lose gram-positivity and show a stippled appearance of gram-positive granules.

AUTHOR'S SUMMARY.

DRIED SERUM FOR DETERMINING BLOOD GROUPS. M. CISLER and N. KOVÁCS, München. med. Wchnschr. **77**:709, 1930.

Favorable results with dried serum are reported, and an improved method of preparing it is described. Properly dried serum may be stored for a long time without loss of potency.

INJECTION METHODS IN EXPERIMENTAL SYPHILIS OF RABBITS. WERNER WORMS, Zentralbl. f. Bakteriol. **114**:355, 1929.

This is an illustrated article discussing operative methods and anatomic relationships for the more accurate study of syphilis in rabbits. References to German textbooks on the anatomy of experimental animals are given.

PAUL R. CANNON.

A METHOD FOR THE DETERMINATION OF THE TOTAL NUMBER OF BACILLI IN SPUTUM. E. BUTSCHOWITZ, Ztschr. f. Tuberk. **55**:321, 1930.

A measured amount of sputum is digested with sodium hydroxide and neutralized. A suspension of yeast cells is added and well mixed. A smear of this mixture is stained for tubercle bacilli, and the relative number of tubercle bacilli and yeast cells is determined. The number of yeast cells in the original suspension is determined by counting in a hematologic counting chamber. These data permit a simple calculation from which to estimate the actual number of tubercle bacilli in the sputum.

MAX PINNER.

Society Transactions

CHICAGO PATHOLOGICAL SOCIETY

Regular Monthly Meeting, Dec. 8, 1930

JOSEPH A. CAPPS, *President, in the Chair*

OSTEITIS FIBROSA IN THE SKELETON OF A PREHISTORIC AMERICAN INDIAN. HENRI S. DENNINGER.

The complete report will be published in the ARCHIVES OF PATHOLOGY.

DISCUSSION

E. R. LONG: The number of studies of diseases of prehistoric inhabitants of this country is limited, and there seems to be considerable opportunity for further research. There is the possibility of gaining information by the study of any calcified masses of tissues and concretions that may be found associated with such skeletons.

PROTECTIVE AND COMPLEMENT-BINDING SUBSTANCES IN THE SERUMS OF PERSONS CONVALESCENT FROM YELLOW FEVER. N. PAUL HUDSON.

Immune substances have been demonstrated in the serums of five persons convalescent from laboratory infections with yellow fever. The serums of four were examined periodically during illness and convalescence, and that of the fifth several months after recovery. Unavoidable circumstances prevented the examination of all at regular intervals.

Protective substances were demonstrated by the survival of monkeys given injections of the serum and then injections of yellow fever virus (monkey blood). The serum of one patient, taken on the third and fourth days after the onset of illness, did not protect, but that taken on the fifth and eighth days did protect; the serum of another patient, taken on the third day, had no effect, but that taken on the sixth and eighth days protected; the serum of the third patient, taken on the second and fourth days, did not protect, but that taken on the seventh day did; the serum of the fourth patient gave no protection on the third day, but had protective properties on the fifth and seventh days, and the serum of the fifth patient, tested several months after recovery, repeatedly demonstrated protective properties. It seems, then, that substances protective against the yellow fever virus appear about the fifth day after the onset of illness.

Frobisher (*Proc. Soc. Exper. Biol. & Med.* **26**:846, 1929, and other articles in press), Davis (in personal communications to the author and in reports to the International Health Division of the Rockefeller Foundation) and Aragão (*Compt. rend. Soc. de biol.* **99**:1341, 1928) have reported experiments with complement fixation. The first two workers were successful, the last not. The following technic was found to give the best results: The antigen is serum from infected monkeys, pooled and dried while frozen, and stored in sealed containers in weighed amounts. It is effective for at least thirteen months. Normal monkey

serum similarly stored has no complement-fixing property. The other reagents are two units of guinea-pig complement, the test serum, two units of rabbit ambocepter, and a 2 per cent suspension of sheep's red blood cells. The total volume is 3 cc. Primary incubation is in the refrigerator at 5 C. for about sixteen hours (over night), and the secondary incubation is in the water bath at 37 C. for one-half hour. In carrying out the test, the antigen is diluted over a range of from 1:20 to 1:1,000; the serum concentration is constant, in a dilution of 1:5. Positive tests frequently manifest a prozone. The usual controls are made.

The results of complement-fixation tests during and after convalescence of the persons here considered were as follows: The serum of one convalescent person gave the first positive reaction in the ninth week after the onset of illness, and continued to give positive reactions for nine months after the attack; the serum of the second convalescent person fixed complement in the eighth week and not before; the serum of the third gave a definite, but not strong, reaction in the thirteenth week, in the only examination made thus far; that of the fourth repeatedly failed to fix complement seven months after the onset of the illness; and the serum of the fifth, tested for the first time eight months after the attack, showed complement fixation and continued to do so twenty months after the illness.

Thus, the serums of four persons convalescent from yellow fever had complement-fixing properties beginning a number of weeks after the acute illness, and the serum of one failed to have these after seven months.

DISCUSSION

PAUL CANNON: Does the serum protect if given after the infecting dose; and if so, within what length of time must it be given?

H. P. HUDSON: If the protective serum and the infecting dose are given simultaneously, the animal lives; but if the serum is given as much as twenty-four hours after the infecting dose, there is no protection in monkeys. Protective serum given before the infecting dose is effective for six weeks.

MELANOCARCINOMA OF THE GALLBLADDER. S. R. ROSENTHAL.

A colored man, aged 48, entered Cook County Hospital completely disoriented. According to his wife, he had been in this condition for two days. The only additional information was that he had had lumbar pain and hematuria for two months. The physical examination revealed a bilateral papilledema with hemorrhages, a right lower facial paralysis and absence of abdominal and left cremasteric reflexes. The coordination was poor, and the patient fell to the left side. The spinal fluid was bloody and under increased pressure, and the result of the Wassermann test was strongly positive. The urine was unchanged. The patient died thirteen days after the onset of the cerebral symptoms.

Postmortem examination revealed a pedunculated primary melanocarcinoma of the gallbladder with metastases to the brain, lungs, jejunum and left kidney. All other possible primary sites of melanotic tumors were excluded, such as the skin, the meninges, the brain, the eyes and the rectum.

This report emphasizes that melanotic tumors are epithelial in origin, and that the melanin is formed in the cytoplasm of these cells, as a uniform, finely or coarsely granular pigment varying in color from light to dark brown. In contrast with this conclusion, the cytoplasm of the chromatophores of Ribbert contained an irregular, coarsely granular pigment ranging from dark brown to black.

The complete report will be published in the *American Journal of Cancer*.

RUPTURED ANEURYSM OF THE CYSTIC ARTERY OF THE GALLBLADDER AS A RESULT OF TOXIC ARTERITIS. S. R. ROSENTHAL.

The complete report will be published in the ARCHIVES OF PATHOLOGY.

PATHOLOGIC DISSIMILARITY IN TWO CLINICALLY SIMILAR CASES OF BLOOD DYSCRASIA. L. BLEYER and CHARLES ULRICH.

The complete clinical records and the results of examinations of the blood of two patients are reported, with a brief review of the literature. One patient had acute lymphatic leukemia, which terminated fatally within a week, and another had so-called "infectious mononucleosis," which progressed slowly to complete clinical recovery after eight months. The blood, however, still shows slight abnormalities.

The similarities and dissimilarities in the blood of these patients were discussed. Infectious mononucleosis may represent a functional lability of the lymphatic system, with a possible predisposition to lymphatic leukemia in later life. Examinations of the blood of patients with this condition should be made over a sufficient length of time to determine the ultimate outcome.

The complete report appeared in J. A. M. A. **96**:191 (Jan. 17) 1931.

DISCUSSION

JOSEPH A. CAPPS: Patients with "mononucleosis" have great clinical interest. I have thought that these cells probably came from the reticulo-endothelial system rather than from the lymphoid tissues. They are seen in the blood with a great many diseases.

R. H. JAFFÉ: Supravital stains are necessary to determine more accurately the nature of these cells.

MUCOCELE OF THE APPENDIX, WITH A DIVERTICULUM AND INVAGINATION INTO THE CECUM. F. W. MULSOW.

Mucocele of the appendix is rare and is seldom recognized clinically. It is found most often during postmortem examinations or during operations for chronic abdominal conditions, and in the male is the most frequent cause of pseudomyxoma peritonei. Phemister (*J. A. M. A.* **84**:1834, 1925) stated that an acute inflammation requiring immediate surgical relief rarely develops. Other complications are intussusception, invagination, volvulus, intestinal obstruction and hernia. Dodge (*Ann. Surg.* **63**:335, 1916) found 142 reports, of which 55 were based on tissues obtained postmortem, 66 on tissues obtained by operations, and 21 on cases without these details. Chronic inflammation was reported in 45, diverticuli in 12 and pseudomyxoma peritonei in 14. Weaver (*California & West. Med.* **29**:500, 1928) stated that 168 reports had been recorded. Since then Topping (*California & West. Med.* **29**:186, 1928) and Vorhaus (*J. A. M. A.* **94**:165, 1930) have added two more.

This condition is due usually to constriction or obliteration of the lumen in the proximal portion of the appendix by scar tissue, a neoplasm or a kink at the base. In most instances the lumen is obliterated, and the retained material is a stérile, viscid secretion. In the case reported by Vorhaus, barium was demonstrated in the lumen by the x-ray film. Castle (*Ann. Surg.* **61**:582, 1916) thought that the lesion in his patient may have resulted from the scarring of typhoid ulcers. Phemister attempted to reproduce the condition in dogs by closing the lumen, but acute appendicitis developed or the lumen was reestablished. A discussion and review of the size, shape, chemical contents, occurrence, etiology, morbid anatomy, diagnosis, etc., has been made by Morrison (*Boston M. & S. J.* **188**:533, 1923) so that further discussion of these points seems unnecessary. I have not found in the literature a report similar to the account here given, in which invagination of the appendix into the cecum with resulting gangrene of the cecum is described.

A man, 47 years of age, without previous gastro-intestinal disturbances, except typhoid fever at the age of 14 years, had, in 1926, a right inguinal hernia, which healed in about one year with the use of a truss. During the months of April and May, 1928, he had several attacks of pain and distress in the lower right

quadrant of the abdomen, which seemed to be relieved by rest or by the use of laxatives. During the following summer he had no further symptoms, and his bowels moved regularly without laxatives. About the middle of November, 1928, the pain and abdominal distress returned. He noticed in the lower right quadrant of the abdomen, a hard, tender mass, which did not disappear with the use of laxatives. He consulted his physician on Dec. 5, 1928, who noticed the tender mass in the region of the appendix. There was no nausea or fever. After three days without relief the patient entered the hospital. The surgeon found the abdomen flat, that there was no rigidity of the muscles, and that a palpable, tender mass was present in the region of the appendix. The temperature was 102 F., and the blood contained 17,000 leukocytes per cubic millimeter. The clinical diagnosis was acute appendicitis with a possible abscess.

The surgeon found that the spherical enlargement of the proximal end of the appendix had invaginated into the cecum. The pressure had impaired the blood supply to the cecum and had caused gangrene, especially of that portion covering the proximal end of the enlarged appendix. The appendix and the gangrenous portion of the cecum were removed, and the patient made an uneventful recovery.

The appendix was 9.5 cm. long. The spherical proximal portion was 4 cm. in diameter, and the remaining part was 5.5 cm. long and 2.2 cm. in diameter. Near the distal end, along the mesentery, was a large diverticulum, which was 2 cm. in diameter at the base and which projected 1.3 cm. The blood vessels of the serosa of the appendix were distended with blood. The mucosa of the cecum covering the tissues invaginated into the cecum was discolored and gangrenous. The wall of the diverticulum was less than 1 mm. thick. The wall of the appendix was 5 mm. thick, and that of the spherical part was from 3 to 4 mm. thick. The lumen was filled with a clear, gelatinous material, in which were a few gray threads. There was no lumen in the proximal end. The wall of the diverticulum consisted of a thin layer of connective tissue, covered with a serous surface. There were extensive scarring of the wall of the appendix and hypertrophy of the smooth muscle tissues. Only small portions of the mucosa had lining epithelial cells. Secreting epithelial cells were not found. There were acute inflammation and necrosis of the wall of the cecum covering the invaginated part of the appendix.

Mucocele of the appendix is rarely an acute surgical condition. The presence of a diverticulum of a mucocele is even more rare and is very suggestive of the method of development from an appendix, of the condition known as pseudomyxoma peritonei. The invagination of such an appendix into the cecum with resulting gangrene of the cecum is a rare condition; at least no similar report was found in the available literature.

Book Reviews

A Text-Book of Histology. By Alexander A. Maximow, Late Professor of Anatomy, University of Chicago. Completed and Edited by William Bloom, Assistant Professor of Anatomy, University of Chicago. Cloth. Price, $9. Pp. 833, with 604 illustrations, some in colors. Philadelphia: W. B. Saunders Company, 1930.

From the preface we learn that at the time of his death in December, 1928, Professor Maximow was writing a textbook of histology. Much material and many illustrations had been collected. The sections on the generative organs, the urinary tract, the organs of special sense and epithelium had been completed. The sections on the blood and connective tissue, the gastro-intestinal tract, the vascular and lymphatic systems, the spleen, the skin and the mammary gland were left in rough manuscript. The book has been completed and edited by William Bloom, who has written the sections on the biliary and respiratory systems, the pancreas, the endocrine glands with the exception of the suprarenals (which are described by N. Hoerr) and the introductory chapter. With the help of Prof. C. Judson Herrick he has also compiled, from various sources, including a Russian text by Professor Maximow, the chapters on the nervous tissues. Professor Bloom deserves a great deal of credit and praise for his faithful and arduous work without which the book could not have been completed. The result is a magnificent textbook of histology, superbly illustrated, which in general reflects faithfully the ideas of its masterful originator. The book is based so far as possible, with respect to both text and illustrations, on human material. It covers the field of histology completely, except that it does not include placentation and general embryology or the detailed structure of the brain and the spinal cord. However, it does include a description of the histogenesis of tissues and organs whenever it aids in understanding the mature structure. Technical matters and, in large measure, bibliographic references have been omitted in order to avoid much unnecessary duplication of matter already in print. The functional aspects of the structures described are not neglected, but receive interesting consideration under the heading "Histophysiologic Remarks." The style is clear and vigorous. As is well known, Professor Maximow was an active champion of the so-called unitarian theory of the formation of blood and connective tissue, and the results he obtained in his splendid work on vital staining and on the cultivation of tissue were interpreted in the light of this theory. The cells and tissues in question, their interrelationships and potentialities and other problems are considered in detail in chapters 3, 4 and 5, which deal with blood and connective tissue, and with blood-forming and blood-destroying tissue. Many pathologists will be greatly interested in these chapters, and the book will be an invaluable help to the student of pathologic histology and histogenesis.

Legal Medicine and Toxicology. By Ralph W. Webster, M.D., Ph.D., Late Clinical Professor of Medicine (Medical Jurisprudence) in Rush Medical College, University of Chicago, Chicago. Cloth. Price, $8.50. Pp. 862, with illustrations. Philadelphia: W. B. Saunders Company, 1930.

The object of this book, by the late Dr. Ralph W. Webster, is "to present in one volume the more usual phases of Legal Medicine in a somewhat concise manner, in order that the busy practitioner may have access to the more important points involved in the cases with which he, ordinarily, comes in contact and upon which he may be called upon to inform himself before giving testimony in such cases; and, also, in order that the student may have a presentation before

him, so that he may be able to learn the rudiments of the science and may prepare himself for the different examinations for licensure."

After an introductory chapter dealing with definitions, ordinary and expert witnesses and legal procedure, the volume is divided into two parts. Part I, Legal Medicine, occupies slightly less than 300 pages and deals with such subjects as legal rights and obligations of physicians, malpractice, identification of the living and the dead, postmortem observations characteristic of death from various causes, wounds and their medicolegal aspects, examination of blood stains, etc. These subjects are considered briefly, but perhaps adequately for the purposes of the book. Part II, Toxicology, consists of more than 500 pages. In his preface the author states that the apparent undue stress laid on toxicology in this work is due to the fact that he "has thought it advisable to go much more thoroughly into the methods of isolation and identification of the various poisons discussed than is the case with other single-volume works on the subject." Numerous cases of poisoning, sometimes on a wholesale scale, are cited. The commoner poisons are discussed in considerable detail; for example, about 65 pages are occupied by the discussion of arsenic.

The illustrations are not numerous and are not especially distinctive. References to the literature are reasonably abundant. The typography is satisfactory. A well arranged table of contents of ten pages is inserted at the beginning, and a full index of thirty-one pages at the end of the book.

This volume does what the author stated was his object, as quoted at the beginning of this review. It can therefore be recommended to those in need of a reliable and fairly brief textbook on the subject of legal medicine and toxicology.

DER APPENDICITISCHE ANFALL SEINE ATIOLOGIE UND PATHOGENESE. By LUDWIG ASCHOFF. Mit Einem Kurzen Beitrag über die Lymphgefassverhaltnisse am Menschlichen Wurmfortsatz von Dr. H. Seng. Price, 12.40 marks. Pp. 125, with 36 illustrations. Berlin: Julius Springer, 1930.

This is the first in a new series of monographs on clinicophysiologic problems considered particularly from the anatomic and pathologico-anatomic point of view. The problems may lie in any part of normal and pathologic anatomy on the one hand and in the clinical or pathologic physiology on the other hand, but they are to illustrate the relationship between the morphologic and the physiologic lines of thought, and in each case the problem will be discussed by an active investigator in the field in question on the basis principally of his own work. Aschoff discusses acute appendicitis, its cause and genesis, in five chapters, the titles of which will indicate the scope of his discussion: anatomic and physiologic preliminaries, including the lymph vessels of the appendix, by H. Seng; investigations of the etiology of appendicitis; the pathogenesis of acute appendicitis; conclusions and clinical hints. The investigations of the etiology includes bacterioscopic studies of smears and of sections of acutely inflamed appendixes as well as cultures. The bacterioscopic studies are regarded as highly significant, because they establish the forms of the bacteria that were subjected to phagocytosis and that consequently may be assumed to be active infectious agents. An important outcome of the bacteriologic work is the demonstration that the bacterial flora of the distal third of the appendix is peculiar and contains the bacteria that are found in the acutely inflamed appendix. The most common bacterial agent in acute appendicitis appears to be the so-called enterococcus or intestinal streptococcus; then come the pneumococcus, the colon bacillus, a small gram-positive rod and an influenza-like rod. It is believed that retention in the distal end increases the virulence of appendical flora and thus favors the acute attack, which is enterogenic and begins on the surface of the mucous membrane. The presentation is clear and simple. The illustrations are excellent. The monograph is an important addition to the literature on acute appendicitis and sets a high standard for the subsequent numbers of the series. Practical pathologists will be interested especially in the instructive survey of the results of the examination of 1,000 appendixes and in the thoughtful review of errors in clinical diagnosis.

MOLDS, YEASTS, AND ACTINOMYCETES: A HANDBOOK FOR STUDENTS OF BACTERIOLOGY. By ARTHUR T. HENRICI, M.D., Professor of Bacteriology, University of Minnesota. Cloth. Price, $3.50 net. Pp. 296, with 100 illustrations. New York: John Wiley & Sons, Inc., 1930.

This book is the outgrowth of a lecture course that has been offered at the University of Minnesota for some years. It was designed to fill the gap between the brief and inadequate discussions of the fungi found in many textbooks of bacteriology, and the extensive monographs and technical articles which have been written on the particular groups. Henrici has gone far in accomplishing his aim. The discussions of the several groups are necessarily brief, but he has succeeded in presenting much of the newer knowledge. The book will serve a useful purpose as a source of information in a field where few tread with much assurance. It should be of interest to microbiologists working in the various fields of applied microbiology, and especially to medical bacteriologists who have not always shown much familiarity with the uncommon fungi as causes of infections. If Henrici's book will help to drive from usage the terms "blastomyces" and "blastomycosis" alone, its appearance will have been vindicated.

The material is organized in eleven chapters as follows: I. The Structure and Classification of the Fungi; II. Methods for Studying Molds, Yeasts, and Actinomycetes; III. Biological Activities of the Molds; IV. Molds Belonging to the Phycomycetes; V. Molds Belonging to the Ascomycetes and Fungi Imperfecti; VI. The Dermatomycoses; VII. Fungi Transitional Between Molds and Yeasts: Oidium and Monilia; VIII. Morphology and Classification of the Yeasts; IX. Biological Activities of the Yeasts; X. Morphology and Classification of the Actinomycetes; XI. Biological Activities of the Actinomycetes.

Little more need be said about the contents, since the headings of the chapters suffice. The book is to be recommended to students of mycology, who need a general discussion of yeasts, molds and actinomycetes.

SELECTED READINGS IN THE HISTORY OF PHYSIOLOGY. Edited by JOHN FAHRQUHAR FULTON, M.D., Formerly Fellow of Magdalen College, Oxford; Sterling Professor of Physiology, Yale University. Price, $5. Pp. 317, with 60 illustrations. Springfield, Ill.: Charles C. Thomas, 1930.

This book is patterned after Long's "Readings in Pathology" by the same publisher. It reproduces original passages that have exercised a marked influence on the development of physiologic knowledge. In order to secure a desirable sequence in various fields, the readings have been grouped chronologically according to subject as follows: general principles, circulation of the blood, the capillaries, respiration, digestion, muscle and peripheral nerves, the central nervous system and miscellaneous. Each section is preceded by a brief introductory explanation by the editor, who also writes brief but valuable biographic notes of the authors whose works are cited. The passages are taken from the earliest editions of the works in question. Full bibliographic description is given of each publication cited. In all English passages the original spelling and punctuation have been preserved; selections from other languages are given either in contemporary or fresh translations. The sixty illustrations are well chosen and refreshingly unconventional. The publisher's task is well done. From the editor's preface one learns that "of the 65 selections of which information was available concerning the age of the author when the work was done, 11 were written between 20 and 30 years of age — Mayow and de Graaf being 23, Arrhenius 24, and Helmholtz (Conservation of Energy), Blagden, Cannon and Herbert Mayo 26; 23 were written between the ages of 30 and 40 years, and the remaining 42 were written when their authors were over 40." The frequency with which important conclusions have been based on the results of experiments on human beings is also illustrated by the selections. Fulton's "Readings" is a valuable book. To the interested student it will be a stimulus, because it provides direct contact with the original source of great physiologic discoveries and contributions.

A SYSTEM OF BACTERIOLOGY IN RELATION TO MEDICINE. Medical Research Council. Volume 7: Virus Diseases, Bacteriophage. Cloth. Price, per volume, 1 pound, 1 shilling, net. Pp. 509. London: His Majesty's Stationery Office, 1930. (May be obtained from the British Library of Information, 551 Fifth Avenue, New York.)

The first five volumes of the Medical Research Council's system of bacteriology have been received with marked favor. Its standing as a contribution of great value to the literature of bacteriology in relation to medicine may be said to be assured. Volume 7 measures up to the standards of its predecessors. It deals with virus diseases and bacteriophage. Virus diseases of plants, animals and man are discussed in 38 chapters (450 pages) by about 27 British workers in microbiology. Within comparatively small compass are presented valuable critical summaries of the present knowledge of viruses and virus diseases, their nature and causes. About 18 human diseases currently accepted as of the virus class are considered. Apparently the recent outbreaks of parrot fever occurred after the printing of the volume was under way as this fever is not discussed. The statement at the bottom of page 185, about the epidemiology of infantile paralysis in the United States, is highly erroneous and should be corrected so far as possible. The only illustrations in the volume are of cell inclusions in certain virus diseases — "virus bodies" — and changes in the central nervous system in encephalitis and epidemic poliomyelitis. Each chapter is provided with an adequate list of references.

In the last chapter of the volume F. M. Burnet of Melbourne gives a good account of bacteriophage and cognate phenomena.

Books Received

BRIGHT'S DISEASE: OBSERVATIONS ON THE COURSES OF DIFFERENT TYPES AND ON THE RESULTANT CHANGES IN RENAL ANATOMY. By D. D. Van Slyke, Edgar Stillman, Eggert Möller, W. Ehrich, J. F. McIntosh, L. Leiter, E. M. Mackay, R. R. Hannon, N. S. Moore and Christopher Johnston. From the Hospital of the Rockefeller Institute for Medical Research. Medicine Monograph XVIII. Price, $3.00. With 107 illustrations. Baltimore: Williams & Wilkins Company, 1930.

MEDICAL USES OF RADIUM. SUMMARY OF REPORTS FROM RESEARCH CENTRES FOR 1929. Medical Research Council Special Report Series, no. 150. Price, 9 pence. Pp. 32. London: His Majesty's Stationery Office, 1930.

TUBERCULOSIS IN MAN AND LOWER ANIMALS. Medical Research Council Special Report Series, no. 149. By H. H. Scott. Price, 4 shillings. Pp. 270. London: His Majesty's Stationery Office.

THE REGULATION OF SIZE AS ILLUSTRATED IN UNICELLULAR ORGANISMS. By Edward F. Adolph, Ph.D., Associate Professor of Physiology, University of Rochester. Price, $4.50. Pp. 233, with 66 illustrations and 15 tables. Springfield, Ill.: Charles C. Thomas, 1931.

SELECTED READINGS IN THE HISTORY OF PHYSIOLOGY. Edited by John Farquhar Fulton, Jr., M.D., Formerly Fellow of Magdalen College, Oxford; Sterling Professor of Physiology, Yale University. Price, $5.00, postpaid. Pp. 317, with 60 illustrations. Springfield, Ill.: Charles C. Thomas, 1930.

CLINICAL ALLERGY, PARTICULARLY ASTHMA AND HAY FEVER: MECHANISM AND TREATMENT. By Francis M. Rackemann, M.D., Physician to the Massachusetts General Hospital; Instructor in Medicine, Harvard Medical School, Boston. Price, $10.50. Pp. 617, with 30 illustrations. New York: The Macmillan Company, 1931.

DER APPENDICITISCHE ANFALL: SEINE ÄTIOLOGIE UND PATHOGENESE. Von Ludwig Aschoff, Freiburg I.Br. Mit Einem Kurzen Beitrag über die Lymphgefassverhaltnisse am Menschlichen Wurmfortsatz von Dr. H. Seng. Price, unbound, 12.40 marks; bound, 14.00 marks. Pp. 125, with 36 illustrations. Berlin and Vienna: Julius Springer, 1930.

THE ARCHIVES OF PATHOLOGY is published by the American Medical Association as a medium to advance the science of pathology in the United States and for the promotion of research and observation in this field.

Manuscripts for publication, books for review, and correspondence relating to contributions should be sent to Dr. [illegible] Hektoen, 637 South Wood Street, Chicago, or to any other member of the Editorial Board. Communications regarding subscriptions, reprints, etc., should be addressed, ARCHIVES OF PATHOLOGY, American Medical Association, 535 North Dearborn Street, Chicago.

Articles are accepted for publication on condition that they are contributed solely to the ARCHIVES OF PATHOLOGY. Manuscripts must be typewritten, preferably double spaced, and the original copy should be submitted. Zinc etchings and halftones of illustrations will be supplied by the publishers when the original illustrations warrant.

Footnotes and bibliographies should conform to the style of the Quarterly Cumulative Index Medicus, published by the American Medical Association. This requires, in order given: name of author, title of article, name of periodical, with volume, page, month—day of month if weekly—and year. A complete list of abbreviations for standard periodicals, together with a full discussion of the style of the A. M. A. publications, appears in The Art and Practice of Medical Writing, a comprehensive book on the preparation of medical manuscripts, published by the American Medical Association. Price, $1.50.

Matter appearing in the ARCHIVES OF PATHOLOGY is covered by copyright, but, as a rule, no objection will be made to its reproduction in reputable medical journals if proper credit is given. However, the reproduction for commercial purposes of articles appearing in the ARCHIVES OF PATHOLOGY, or in any of the other publications issued by the Association, will not be permitted.

Authors will receive one hundred reprints free; additional reprints may be obtained at cost.

The ARCHIVES OF PATHOLOGY is published monthly. Annual subscription price (two volumes): Domestic, $6.00; Canadian, $6.40; foreign, $6.75, including postage. Single copies, 75 cents, postpaid.

Checks, etc., should be made payable to the AMERICAN MEDICAL ASSOCIATION.

OTHER PERIODICAL PUBLICATIONS
of the American Medical Association

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION—Weekly. Covers all the medical activities and matters of general medical interest. Illustrated. Annual subscription price (two volumes): Domestic, $7.00; Canadian, $8.50; foreign, $8.00. Single copies, 25 cents.

ARCHIVES OF INTERNAL MEDICINE—Monthly. Devoted to the publication of advanced original clinical and laboratory investigations in internal medicine. Illustrated. Annual subscription price (two volumes): Domestic, $5.00; Canadian, $5.40; foreign, $5.75. Single copies, 50 cents.

AMERICAN JOURNAL OF DISEASES OF CHILDREN—Monthly. Presents pediatrics as a medical science and as a social problem. It involves carefully prepared collective abstracts based on recent pediatric literature, abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 65 cents.

ARCHIVES OF NEUROLOGY AND PSYCHIATRY—Monthly. A medium for the presentation of original articles on nervous and mental diseases, with abstracts from foreign and domestic literature, book reviews, society transactions, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY—Monthly. Devoted to advancing the knowledge of and progress in cutaneous diseases and syphilis. Publishes original contributions and full abstracts of the literature on these two subjects, transactions of the important dermatological societies, book reviews, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 65 cents.

ARCHIVES OF SURGERY—Monthly. Devoted largely to the experimental and clinical study of surgery, with monthly reviews of orthopedic and urologic surgery. Well illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

ARCHIVES OF OTOLARYNGOLOGY—Monthly. A medium for the presentation of original articles on diseases of the ear, nose and throat, with abstracts from foreign and domestic literature, book reviews, the transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 75 cents.

ARCHIVES OF OPHTHALMOLOGY—Monthly. Includes original articles on diseases of the eye, abstracts from foreign and domestic literature, book reviews, transactions of special societies, etc. Illustrated. Annual subscription price (two volumes): Domestic, $8.00; Canadian, $8.40; foreign, $8.75. Single copies, 85 cents.

QUARTERLY CUMULATIVE INDEX MEDICUS—Quarterly. A complete subject and author index to the world's medical literature of the world. Issued four times a year. Second and fourth volumes bound for permanent reference. Subscription price, calendar year: Domestic, $12.00; Canadian, $12.60; foreign, $12.75.

AMERICAN MEDICAL ASSOCIATION
535 North Dearborn St. CHICAGO

CONTENTS

PAGE

THE ARGENTOCHROMO-ARGENTAFFIN ... E. PESSIN, M.D., ... 171

EXPERIMENTAL RHEUMATIC LESIONS ... AND IN RABBITS. ... PHILADELPHIA 190

FIBROUS ... (OSTEITIS ... EXPERIMENTAL ... HYPERPARATHYROIDISM OF GUI... HENRY L. JAFFE, ... M.D., ALBON HOLDEN, PH.D., ... E. BLAIR, PH.D., ... 207

INVASION OF THE FALLOPIAN TUBE ... VERMICULARIS: ... CASE. W. J. JONES, ... LA CROSSE, WIS., ... AND CARL BUNTING, M.D., MA... 229

MALIGNANT ... AND SITUATED ON THE ... MAJUS: REPORT ... OF A CASE. JOSEPH McFARLAND, ... PHILADELPHIA 239

THE ... OF BLOOD PLATELETS ... ERNAL STIMULI: ... HISTOLOGIC LIGHT, IODINE ... TAR. PAUL E. ... STEINBERG, S., AND FRANCES D. ... D., CHICAGO 241

THE ... OF INVASION OF ... LS IN ADENOMAS ... OF THE THYROID GLAND. SHIM... M.D., BOSTON. 253

GENERAL REVIEW:

PUBLISHED ... SYPHILIS ITS FRE... ATHOLOGY AND ... HISTOPATHOLOGIC APPEARANCE. ... McINTYRE, M.D., ... ELLSWORTH, MICH. 258

BOOKS AND REPORTS ... 281

ABSTRACTS FROM CURRENT LITERATURE ... 282

PROCEEDINGS OF SOCIETIES:

CHICAGO PATHOLOGICAL SOCIETY ... 326

BOOK ... 330

BOOK ... 334